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SESSION RESUMED IN FILE 'STNGUIDE' AT 14:18:56 ON 27 JAN 2003  
FILE 'STNGUIDE' ENTERED AT 14:18:56 ON 27 JAN 2003  
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.66	7.57
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.65

=> d his

(FILE 'HOME' ENTERED AT 14:00:36 ON 27 JAN 2003)

FILE 'CAPLUS' ENTERED AT 14:00:53 ON 27 JAN 2003  
L1 1 S 130:209820/DN

FILE 'STNGUIDE' ENTERED AT 14:02:50 ON 27 JAN 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.66	7.57
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.65

FILE 'REGISTRY' ENTERED AT 14:19:09 ON 27 JAN 2003  
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STRUCTURE FILE UPDATES: 26 JAN 2003 HIGHEST RN 481631-75-8  
DICTIONARY FILE UPDATES: 26 JAN 2003 HIGHEST RN 481631-75-8

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNnote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 09406269.str

L2 STRUCTURE UPLOADED

=> d

L2 HAS NO ANSWERS

L2 STR

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

Structure attributes must be viewed using STN Express query preparation.

=> s l2

SAMPLE SEARCH INITIATED 14:19:28 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 244 TO ITERATE

100.0% PROCESSED 244 ITERATIONS

2 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 3943 TO 5817

PROJECTED ANSWERS: 2 TO 123

L3 2 SEA SSS SAM L2

=> s l2 full

FULL SEARCH INITIATED 14:19:33 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 4735 TO ITERATE

100.0% PROCESSED 4735 ITERATIONS

53 ANSWERS

SEARCH TIME: 00.00.01

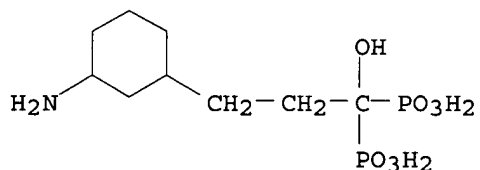
L4 53 SEA SSS FUL L2

=> d scan

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS

IN Phosphonic acid, [3-(3-aminocyclohexyl)-1-hydroxypropylidene]bis- (9CI)

MF C9 H21 N O7 P2



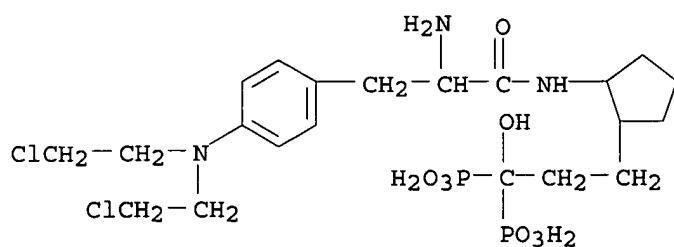
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS

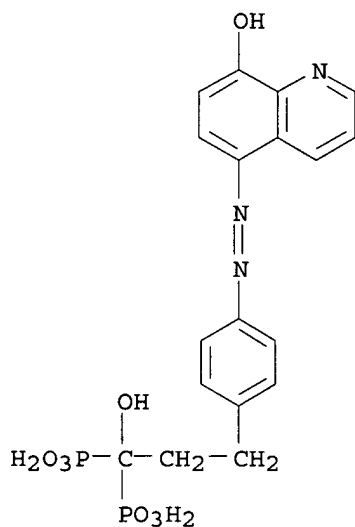
IN Phosphonic acid, [3-[2-[[2-amino-3-[4-[bis(2-chloroethyl)amino]phenyl]-1-oxopropyl]amino]cyclopentyl]-1-hydroxypropylidene]bis- (9CI)

MF C21 H35 Cl2 N3 O8 P2



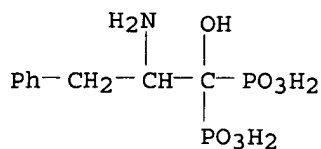
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
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 MF C18 H19 N3 O8 P2

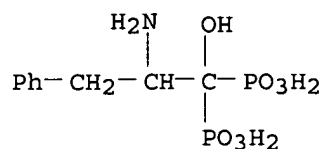


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
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 MF C9 H15 N O7 P2 . Na

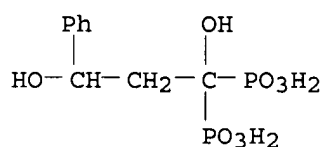


Na



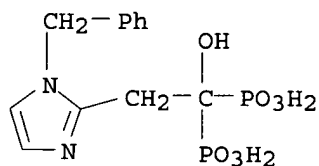
● Na

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
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 MF C9 H14 O8 P2



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

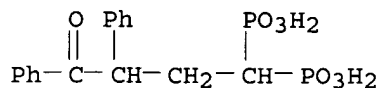
L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
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 MF C12 H16 N2 O7 P2



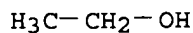
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
 IN Phosphonic acid, (4-oxo-3,4-diphenylbutylidene)bis-, diethyl ester, disodium salt (9CI)  
 MF C20 H26 O7 P2 . 2 Na  
 CI IDS

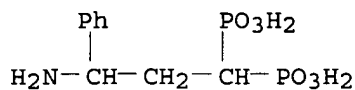
CM 1



CM 2

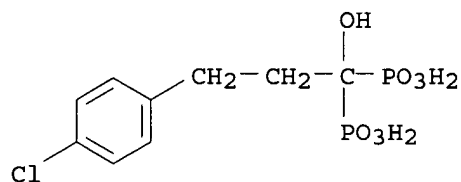


L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
 IN Phosphonic acid, (3-amino-3-phenylpropylidene)bis-, tetrasodium salt (9CI)  
 MF C9 H15 N O6 P2 . 4 Na



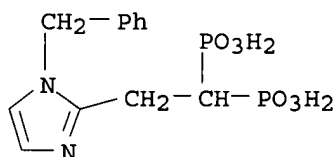
● 4 Na

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
 IN Phosphonic acid, [3-(4-chlorophenyl)-1-hydroxypropylidene]bis- (9CI)  
 MF C9 H13 Cl O7 P2



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

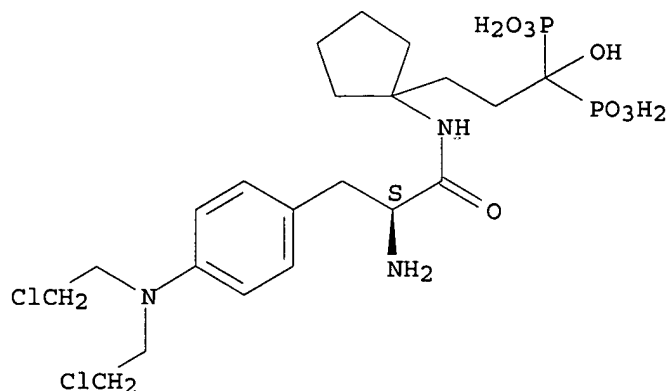
L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
 IN Phosphonic acid, [2-[1-(phenylmethyl)-1H-imidazol-2-yl]ethylidene]bis- (9CI)  
 MF C12 H16 N2 O6 P2



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L4 53 ANSWERS REGISTRY COPYRIGHT 2003 ACS  
 IN Phosphonic acid, [3-[1-[[2-amino-3-[4-[bis(2-chloroethyl)amino]phenyl]-1-oxopropyl]amino]cyclopentyl]-1-hydroxypropylidene]bis-, (S)- (9CI)  
 MF C21 H35 Cl2 N3 O8 P2

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.15

155.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-0.65

FILE 'CAPLUS' ENTERED AT 14:19:52 ON 27 JAN 2003

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FILE COVERS 1907 - 27 Jan 2003 VOL 138 ISS 5

FILE LAST UPDATED: 26 Jan 2003 (20030126/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l4 and (blood or tissue factor or TF or thrombosis)

33 L4

1042405 BLOOD

1131 BLOODS

1042562 BLOOD

(BLOOD OR BLOODS)

546973 TISSUE

275332 TISSUES

706565 TISSUE

(TISSUE OR TISSUES)  
754434 FACTOR  
656539 FACTORS  
1193077 FACTOR

(FACTOR OR FACTORS)  
3685 TISSUE FACTOR  
(TISSUE(W) FACTOR)

9362 TF  
413 TFS  
9633 TF

(TF OR TFS)  
15745 THROMBOSIS

L5 1 L4 AND (BLOOD OR TISSUE FACTOR OR TF OR THROMBOSIS)

=> d ibib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:833023 CAPLUS

DOCUMENT NUMBER: 135:376738

TITLE: Compounds and methods for modulating cerebral amyloid  
angiopathy using inhibitors of an amyloid .beta.  
peptide

INVENTOR(S): Green, Allan M.; Gervais, Francine

PATENT ASSIGNEE(S): Neurochem, Inc., Can.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085093	A2	20011115	WO 2000-IB2078	20001222
WO 2001085093	A3	20020829		
WO 2001085093	C2	20020926		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001084313	A5	20011120	AU 2001-84313	20001222
EP 1251837	A2	20021030	EP 2000-993855	20001222
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR 2000016652	A	20021119	BR 2000-16652	20001222
US 2003003141	A1	20030102	US 2000-747408	20001222
PRIORITY APPLN. INFO.:			US 1999-171877P	P 19991223
			WO 2000-IB2078	W 20001222

OTHER SOURCE(S): MARPAT 135:376738

AB The invention provides methods of inhibiting cerebral amyloid angiopathy (CAA) and treating a disease state characterized by cerebral amyloid angiopathy, e.g., Alzheimer's disease, in a subject using an inhibitor of the 39-40 amino acid amyloid .beta. peptide (A.beta.40). The A.beta.40 inhibitor is selected from, e.g., sulfonic acid derivs., such as ethanesulfonic acid, 1,2-ethanedisulfonic acid, 1-propanesulfonic acid, 1,3-propanedisulfonic acid, 1,4-butanedisulfonic acid, 1,5-pentanedisulfonic acid, 2-aminoethanesulfonic acid, 4-hydroxy-1-butanedisulfonic acid, 1-butanedisulfonic acid, 1-decanedisulfonic acid, 2-propanedisulfonic acid, 3-pentanesulfonic acid, 4-heptanesulfonic



acid, etc., and pharmaceutically acceptable salts thereof or from from phosphonic acid derivs., such as diethylphosphonoacetic acid, phenylphosphonic acid, 3-aminopropylphosphonic acid, propylphosphonic acid, etc. The compds. are formulated in a dispersion system, a liposome formulation, or microspheres using a polymeric matrix. The polymeric matrix is selected from natural polymers, such as albumin, alginate, cellulose derivs., collagen, fibrin, gelatin, and polysaccharides, or synthetic polymers such as polyesters, polyethylene glycol, poloxamers, and polyanhydrides. For example, the ability of compds. of the invention to inhibit CAA was measured in 9 wk old hAPP transgenic mice treated with two different concns. of a compd. of the present invention, 3-amino-1-propanesulfonic acid sodium salt, 100 and 30 mg/kg. Mice were administered the compd. for 8 wk, after which they were sacrificed and their brains were perfused and processed for histol. staining with Thioflavin S. This method may also be used as a screening method for detg. activity of a candidate compd. for inhibiting CAA. The extent of CAA in brain sections obtained from these animals was qual. detd. following staining. The results indicate that the test compd. was effective in (i) reducing the no. of mice showing CAA, and (ii) showing an effect on the severity of the deposition seen in the brain vasculature of these animals.

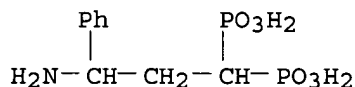
IT 373645-19-3 373645-22-8 373645-36-4  
373645-39-7 373645-41-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors of amyloid .beta. peptide for modulating cerebral amyloid angiopathy)

RN 373645-19-3 CAPLUS

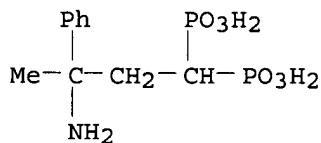
CN Phosphonic acid, (3-amino-3-phenylpropylidene)bis-, tetrasodium salt (9CI)  
(CA INDEX NAME)



●4 Na

RN 373645-22-8 CAPLUS

CN Phosphonic acid, (3-amino-3-phenylbutylidene)bis-, tetrasodium salt (9CI)  
(CA INDEX NAME)

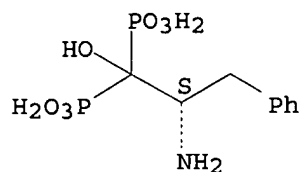


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RN 373645-36-4 CAPLUS

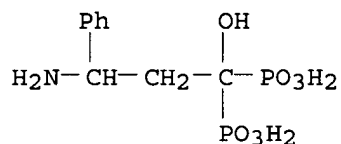
CN Phosphonic acid, [(2S)-2-amino-1-hydroxy-3-phenylpropylidene]bis-, tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●4 Na

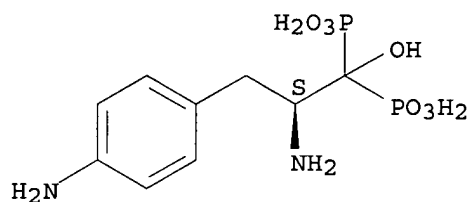
RN 373645-39-7 CAPLUS  
 CN Phosphonic acid, (3-amino-1-hydroxy-3-phenylpropylidene)bis-, tetrasodium salt (9CI) (CA INDEX NAME)



●4 Na

RN 373645-41-1 CAPLUS  
 CN Phosphonic acid, [(2S)-2-amino-3-(4-aminophenyl)-1-hydroxypropylidene]bis-, tetrasodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●4 Na

=> d his

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FILE 'CAPLUS' ENTERED AT 14:00:53 ON 27 JAN 2003

L1 1 S 130:209820/DN

FILE 'STNGUIDE' ENTERED AT 14:02:50 ON 27 JAN 2003

FILE 'REGISTRY' ENTERED AT 14:19:09 ON 27 JAN 2003

L2 STRUCTURE UPLOADED

L3 2 S L2

L4 53 S L2 FULL

FILE 'CAPLUS' ENTERED AT 14:19:52 ON 27 JAN 2003

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 2 Jan 25 BLAST(R) searching in REGISTRY available in STN on the Web  
NEWS 3 Jan 29 FSTA has been reloaded and moves to weekly updates  
NEWS 4 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update frequency  
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02  
NEWS 6 Mar 08 Gene Names now available in BIOSIS  
NEWS 7 Mar 22 TOXLIT no longer available  
NEWS 8 Mar 22 TRCTHERMO no longer available  
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/Caplus and USPATFULL  
NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY  
NEWS 11 Apr 02 PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.  
NEWS 12 Apr 08 "Ask CAS" for self-help around the clock  
NEWS 13 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area  
NEWS 14 Apr 09 ZDB will be removed from STN  
NEWS 15 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB  
NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS  
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available  
NEWS 19 Jun 03 New e-mail delivery for search results now available  
NEWS 20 Jun 10 MEDLINE Reload  
NEWS 21 Jun 10 PCTFULL has been reloaded  
NEWS 22 Jul 02 FOREGE no longer contains STANDARDS file segment  
  
NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002  
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NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 14:34:46 ON 05 JUL 2002

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 14:35:02 ON 05 JUL 2002  
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FILE COVERS 1907 - 5 Jul 2002 VOL 137 ISS 2  
FILE LAST UPDATED: 4 Jul 2002 (20020704/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s 6881-57-8 and pharmaceutical

**REGISTRY INITIATED**

Substance data SEARCH and crossover from CAS REGISTRY in progress...  
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L2 120 L1

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68076 PHARMACEUTICALS  
197679 PHARMACEUTICAL  
(PHARMACEUTICAL OR PHARMACEUTICALS)

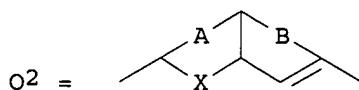
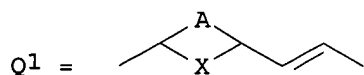
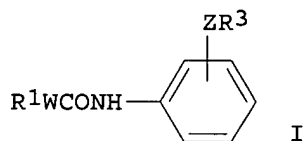
L3 3 L2 AND PHARMACEUTICAL

=> d ibib abs 1-3

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:421562 CAPLUS  
DOCUMENT NUMBER: 131:87834  
TITLE: Preparation of benzoxepinecarboxamides,  
benzocycloheptenecarboxamides,  
naphthalenecarboxamides, and related compounds as CCR5  
antagonists.  
INVENTOR(S): Nishimura, Osamu; Baba, Masanori; Sawada, Hidekazu;  
Kanzaki, Naoyuki; Kuroshima, Ken-ichi; Shiraishi,  
Mitsuru; Aramaki, Yoshio  
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan  
SOURCE: PCT Int. Appl., 516 pp.

CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932100	A2	19990701	WO 1998-JP5708	19981217
WO 9932100	A3	19990910		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304959	AA	19990701	CA 1998-2304959	19981217
AU 9916831	A1	19990712	AU 1999-16831	19981217
ZA 9811574	A	20000619	ZA 1998-11574	19981217
EP 1039899	A2	20001004	EP 1998-961384	19981217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9813691	A	20001010	BR 1998-13691	19981217
JP 2000128782	A2	20000509	JP 1998-360820	19981218
US 6096780	A	20000801	US 1999-377040	19990819
US 6376536	B1	20020423	US 2000-580270	20000526
NO 2000003179	A	20000619	NO 2000-3179	20000619
US 6268354	B1	20010731	US 2000-661320	20000913
PRIORITY APPLN. INFO.:				
			JP 1997-351480	A 19971219
			JP 1998-218875	A 19980803
			JP 1998-234388	A 19980820
			US 1998-104845P	P 19981016
			US 1998-104847P	P 19981116
			US 1998-213377	A3 19981217
			WO 1998-JP5708	W 19981217
			US 1999-377040	A3 19990819
OTHER SOURCE(S): MARPAT 131:87834				
GI				



AB A pharmaceutical compn. for antagonizing CCR5 comprises I [R1 = (substituted) 5-6 membered ring; W = Q1, Q2; A = atoms to form a (substituted) 5-6 membered arom. ring; X = S, O, (substituted) C, N; B = atoms to form a (substituted) 5-7 membered ring; Z = bond, divalent group; R2 = (substituted) amino, ammonio, heterocyclyl, S-bonded group, P(O)kR5R6; k = 0, 1; R5, R6 = (substituted) hydrocarbonyl, amino; PR5R6 = cyclic group]. Thus, 7-(4-methylphenyl)-2,3-dihydro-1-benzoxepine-4-carboxylic acid in CH2Cl2 was treated with (COCl)2 and DMF to give a

residue which was stirred with 4-[N-methyl-N-(tetrahydropyran-4-yl)aminomethyl]aniline and Et<sub>3</sub>N in THF to give N-[4-[N-methyl-N-(tetrahydropyran-4-yl)aminomethyl]phenyl]-7-(4-methylphenyl)-2,3-dihydro-1-benzoxepine-4-carboxamide (II). A II capsule compn. is given.

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:365054 CAPLUS  
DOCUMENT NUMBER: 129:53610  
TITLE: Inhibiting undesirable taste in oral compositions  
INVENTOR(S): Nelson, Sandra Lynn; Walden, Gary Lyle; Hayes, Jeffrey Charles  
PATENT ASSIGNEE(S): Procter + Gamble Company, USA  
SOURCE: Eur. Pat. Appl., 14 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

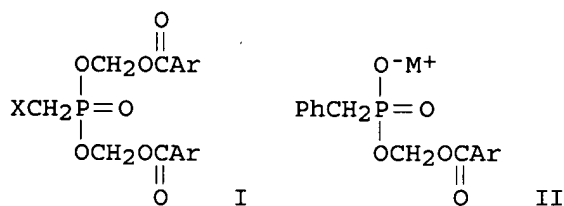
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 845217	A1	19980603	EP 1997-309034	19971111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1996-752088 19961120

AB The present invention relates to a method for inhibiting an undesirable taste in oral compns. such as foods, beverages, dental compns., and **pharmaceuticals**. The present invention also relates to oral and **pharmaceutical** compns. comprising undesirable tasting compds. wherein undesirable tastes are inhibited by the addn. of an inhibitor of intracellular phosphatase enzymes of taste cells to said oral and **pharmaceutical** compns. Said inhibitor is selected from phosphates, thiophosphates, phosphonates, vanadates, bisphosphates, bisphosphonates, phosphate-phosphonates, thiophosphate-phosphates, thiophosphate-phosphonates, their physiol.-relevant salts and esters, and mixts. thereof.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:164348 CAPLUS  
DOCUMENT NUMBER: 120:164348  
TITLE: Synthesis and bioactivation of bis(aroyloxymethyl) and mono(aroyloxymethyl) esters of benzylphosphonate and phosphonoacetate  
AUTHOR(S): Thomson, William; Nicholls, Dave; Mitchell, Antony G.; Corner, Julie A.; Irwin, William J.; Freeman, Sally  
CORPORATE SOURCE: Dep. Pharm. Biol. Sci., Aston Univ., Aston Triangle/Birmingham, B4 7ET, UK  
SOURCE: J. Chem. Soc., Perkin Trans. 1 (1993), (19), 2303-8  
CODEN: JCPRB4; ISSN: 0300-922X  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB The bis(aryloxymethyl) esters of benzylphosphonate, I (X = Ph, Ar = Ph, 2-MeC6H4 or 2,4,6-Me3C6H2), and methoxycarbonylmethylphosphonate, I (X = MeO2C, Ar = Ph, 2-MeC6H4 or 2,4,6-Me3C6H2), have been prepd. by reaction of 2 equiv. of the appropriate aryloxymethyl iodide with the disilver salt of either benzylphosphonate or methoxycarbonylmethylphosphonate. The cyclohexylammonium salts of the mono(aryloxymethyl) esters of benzylphosphonate, II (Ar = Ph, 2-MeC6H4 or 2,4,6-Me3C6H2, M+ = C6H11NH3+), were prepd. by reaction of silver benzyl benzylphosphonate with the appropriate aryloxymethyl iodide, with subsequent hydrogenolysis to remove the P-OCH2Ph group. The bis(aryloxymethyl) esters I (X = Ph or MeO2C, Ar = Ph, 2-MeC6H4 or 2,4,6-Me3C6H2) and the mono(aryloxymethyl) salts II (Ar = Ph, 2-MeC6H4 or 2,4,6-Me3C6H2, M+ = C6H11NH3+) were stable towards chem. hydrolysis at 37.degree. at physiol. pH. In the presence of porcine liver carboxyesterase, the bis(aryloxymethyl) esters of benzylphosphonate I (X = Ph, Ar = Ph or 2-MeC6H4) degraded to the mono(aryloxymethyl) esters II (Ar = Ph or 2-MeC6H4), which showed slow hydrolysis to benzylphosphonate. For the bis(aryloxymethyl) esters of methoxycarbonylmethylphosphonate I (X = MeO2C, Ar = Ph or 2-MeC6H4) there was competition between the esterase-catalyzed hydrolyses of the aryloxymethyl and methoxycarbonyl groups. For the triester I (X = MeO2C, Ar = 2,4,6-Me3C6H2) cleavage of the methoxycarbonyl group was obsd.; hydrolysis of the sterically hindered 2,4,6-trimethylbenzoyl group was not detected for any compd. In regard to aiding charged drug transport across biol. membranes, the authors conclude that, unless a very slow release of parent drug is required, the aryloxymethyl prodrug approach tested here does not offer any apparent advantage over acyloxymethyl or 4-acyloxybenzyl esters already described for several drugs contg. phospho groups.

=> d his

(FILE 'HOME' ENTERED AT 14:34:46 ON 05 JUL 2002)

FILE 'CAPLUS' ENTERED AT 14:35:02 ON 05 JUL 2002  
S 6881-57-8/REG# AND PHARMACEUTICAL

FILE 'REGISTRY' ENTERED AT 14:35:28 ON 05 JUL 2002

L1 1 S 6881-57-8/RN

FILE 'CAPLUS' ENTERED AT 14:35:28 ON 05 JUL 2002

L2 120 S L1

L3 3 S L2 AND PHARMACEUTICAL

=> s l2 and (blood or disease)

980345 BLOOD

1126 BLOODS

980525 BLOOD

(BLOOD OR BLOODS)

535852 DISEASE

137920 DISEASES

604636 DISEASE

(DISEASE OR DISEASES)

L4 2 L2 AND (BLOOD OR DISEASE)

=> d ibib abs hitstr 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS

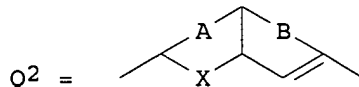
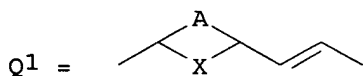
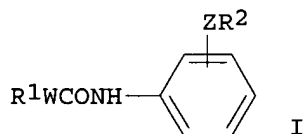
ACCESSION NUMBER: 1999:421672 CAPLUS

DOCUMENT NUMBER: 131:73571

TITLE: Preparation of benzoxepinecarboxamides, benzocycloheptenecarboxamides, naphthalenecarboxamides, and related compounds as MCP-1 receptor antagonists.

INVENTOR(S): Shiraishi, Mitsuru; Kitayoshi, Takahito; Aramaki, Yoshio; Honda, Susumu; Oda, Tsuneo  
 PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan  
 SOURCE: PCT Int. Appl., 513 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932468	A1	19990701	WO 1998-JP5707	19981217
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9813686	A	20001010	BR 1998-13686	19981212
CA 2311428	AA	19990701	CA 1998-2311428	19981217
AU 9916830	A1	19990712	AU 1999-16830	19981217
AU 742077	B2	20011213		
ZA 9811576	A	20000619	ZA 1998-11576	19981217
EP 1040103	A1	20001004	EP 1998-961383	19981217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6166006	A	20001226	US 1998-213379	19981217
JP 11263764	A2	19990928	JP 1998-360780	19981218
NO 2000003133	A	20000809	NO 2000-3133	20000616
US 6413947	B1	20020702	US 2000-661194	20000913
PRIORITY APPLN. INFO.:			JP 1997-351481	A 19971219
			US 1998-213379	A3 19981217
			WO 1998-JP5707	W 19981217
OTHER SOURCE(S):			MARPAT 131:73571	
GI				



AB Title compds. I [R<sub>1</sub> = (substituted) 5-6 membered ring; W = Q<sub>1</sub>, Q<sub>2</sub>; A = atoms to form a (substituted) 5-6 membered arom. ring; X = S, O, (substituted) C, N; B = atoms to form a (substituted) 5-7 membered ring; Z = bond, divalent group; R<sub>2</sub> = (substituted) amino, ammonio, heterocyclyl, S-bonded group, P(O)kR<sub>5</sub>R<sub>6</sub>; k = 0, 1; R<sub>5</sub>, R<sub>6</sub> = (substituted) hydrocarbonyl, amino; PR<sub>5</sub>R<sub>6</sub> = cyclic group], were prepd. Thus, 7-(4-methylphenyl)-2,3-dihydro-1-benzoxepine-4-carboxylic acid in CH<sub>2</sub>Cl<sub>2</sub> was treated with (COCl)<sub>2</sub> and DMF to give a residue which was stirred with 4-[N-methyl-N-(tetrahydropyran-4-yl)aminomethyl]aniline and Et<sub>3</sub>N in THF to give N-[4-[N-methyl-N-(tetrahydropyran-4-yl)aminomethyl]phenyl]-7-(4-methylphenyl)-2,3-dihydro-1-benzoxepine-4-carboxamide (II). II at 1 .mu.M inhibited MCP-1 induced chemotaxis in CHO cells by 89%. A II capsule compn. is given.



IT 6881-57-8P, Benzylphosphonic acid  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. of benzoxepinecarboxamides, benzocycloheptenecarboxamides,  
naphthalenecarboxamides, and related compds. as MCP-1 receptor  
antagonists)  
RN 6881-57-8 CAPLUS  
CN Phosphonic acid, (phenylmethyl)- (9CI) (CA INDEX NAME)

Ph-CH<sub>2</sub>-PO<sub>3</sub>H<sub>2</sub>

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1988:570552 CAPLUS  
DOCUMENT NUMBER: 109:170552  
TITLE: Study of calcium inhibitors of an oxygenated  
heterocycle series.  
AUTHOR(S): Mouysset, G.; Bellan, J.; Payard, M.;  
Tisne-Versailles, J.  
CORPORATE SOURCE: Fac. Pharm., Univ. Toulouse, Toulouse, Fr.  
SOURCE: Farmaco, Ed. Sci. (1987), 42(11), 805-13  
CODEN: FRPSAX; ISSN: 0430-0920  
DOCUMENT TYPE: Journal  
LANGUAGE: French  
AB Seven RCH<sub>2</sub>P(O)(OEt)<sub>2</sub> (I; R = Ph, 2-naphthyl, 2-benzofuryl, etc.) were  
prepd. from RCH<sub>2</sub>Cl and P(OEt)<sub>3</sub>. Hydrolysis of I gave RCH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub> (II). I and  
II showed lower Ca inhibitory activity than did Fostedil.  
IT 6881-57-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn., hydrolysis, and calcium inhibitory activity of)  
RN 6881-57-8 CAPLUS  
CN Phosphonic acid, (phenylmethyl)- (9CI) (CA INDEX NAME)

Ph-CH<sub>2</sub>-PO<sub>3</sub>H<sub>2</sub>

=> s 1/p  
'P' IS NOT A VALID FIELD CODE  
L5 0 1/P

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COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	23.74	24.73
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.10	-3.10

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STRUCTURE FILE UPDATES: 4 JUL 2002 HIGHEST RN 437552-19-7  
DICTIONARY FILE UPDATES: 4 JUL 2002 HIGHEST RN 437552-19-7

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L6 801287 1/P

=> s l6 and phosphonic acid

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5470217 ACID

7807 ACIDS

5475900 ACID

(ACID OR ACIDS)

101684 PHOSPHONIC ACID

(PHOSPHONIC(W) ACID)

L7 80370 L6 AND PHOSPHONIC ACID

=> s 1/nr

L8 2810784 1/NR

=> s l7 and l8

L9 25016 L7 AND L8

=> s l9 and (phenyl or benzyl)

8010973 PHENYL

14 PHENYLS

8010973 PHENYL

(PHENYL OR PHENYLS)

201191 BENZYL

8 BENZYL

201191 BENZYL

(BENZYL OR BENZYL)

L10 12910 L9 AND (PHENYL OR BENZYL)

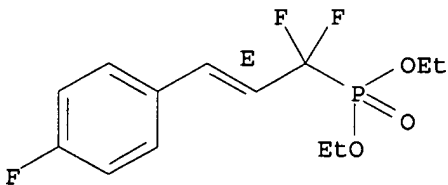
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L10 12910 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Phosphonic acid, [(2E)-1,1-difluoro-3-(4-fluorophenyl)-2-propenyl]-, diethyl ester (9CI)

MF C13 H16 F3 O3 P

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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4688 ESTERS

3587090 ESTER

(ESTER OR ESTERS)

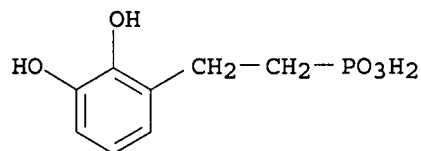
L11 2322 L10 NOT ESTER

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L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Phosphonic acid, [2-(2,3-dihydroxyphenyl)ethyl]- (9CI)

MF C8 H11 O5 P



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

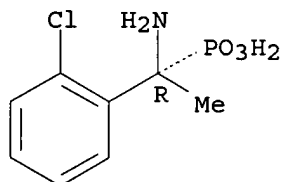
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L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Phosphonic acid, [(1R)-1-amino-1-(2-chlorophenyl)ethyl]- (9CI)

MF C8 H11 Cl N O3 P

Absolute stereochemistry.

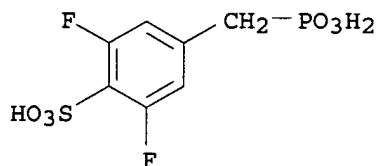


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Benzenesulfonic acid, 2,6-difluoro-4-(phosphonomethyl)- (9CI)

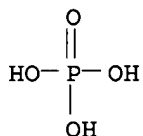
MF C7 H7 F2 O6 P S



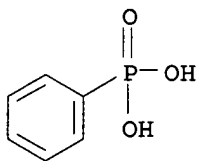
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
 IN Phosphoric acid, zirconium(4+) salt, compd. with phenylphosphonic  
 acid (10:5:4), pentahydrate (9CI)  
 MF C6 H7 O3 P . 5/2 H3 O4 P . 5/4 H2 O . 5/4 Zr

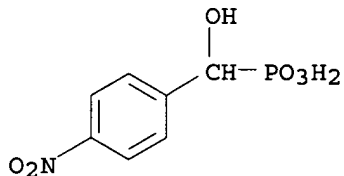
CM 1



CM 2



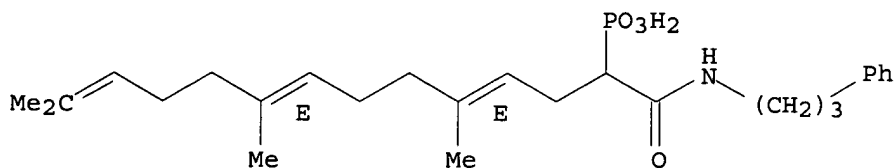
L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
 IN Phosphonic acid, [hydroxy(4-nitrophenyl)methyl]- (9CI)  
 MF C7 H8 N O6 P



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

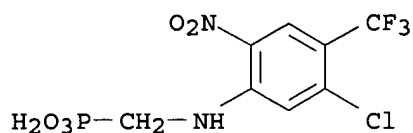
L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
 IN Phosphonic acid, [4,8,12-trimethyl-1-[[[3-phenylpropyl)amino]carbonyl]-3,7,11-tridecatrienyl]-, (E,E)- (9CI)  
 MF C26 H40 N O4 P

Double bond geometry as shown.



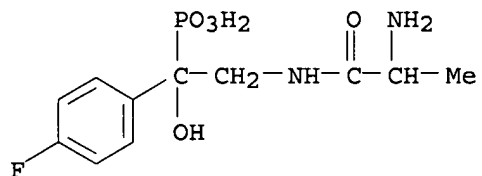
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN Phosphonic acid, [[5-chloro-2-nitro-4-(trifluoromethyl)phenyl]amino]methyl]- (9CI)  
MF C8 H7 Cl F3 N2 O5 P



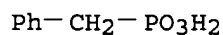
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN Phosphonic acid, [2-[[2-amino-1-oxopropyl]amino]-1-(4-fluorophenyl)-1-hydroxyethyl]- (9CI)  
MF C11 H16 F N2 O5 P



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN Phosphonic acid, (phenylmethyl)-, lanthanum(3+) salt (2:1), dihydrate (9CI)  
MF C7 H9 O3 P . H2 O . 1/2 La

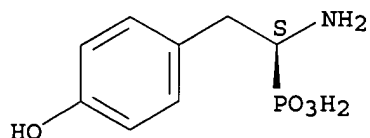


1/2 La(III)



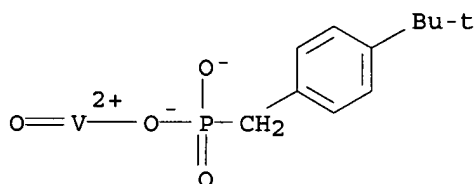
L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN Phosphonic acid, [1-amino-2-(4-hydroxyphenyl)ethyl]-, hydrochloride, (S)- (9CI)  
MF C8 H12 N O4 P . Cl H

Absolute stereochemistry.



● HCl

L11 2322 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN Vanadium, [[4-(1,1-dimethylethyl)phenyl]methyl]phosphonato(2-)-O]oxo-  
(9CI)  
MF C11 H15 O4 P V  
CI CCS, COM



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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0 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

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37085937 1/NC

L12 1612 L11 AND 1/NC

=> s l12 not m/els

3301444 M/ELS

L13 1585 L12 NOT M/ELS

=> s l13 and 3/o

2973275 3/O

L14 643 L13 AND 3/O

=> file caplus

COST IN U.S. DOLLARS

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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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FILE COVERS 1907 - 5 Jul 2002 VOL 137 ISS 2  
FILE LAST UPDATED: 4 Jul 2002 (20020704/ED)

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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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      68076 PHARMACEUTICALS
      197679 PHARMACEUTICAL
          (PHARMACEUTICAL OR PHARMACEUTICALS)
L15      1 L14 (L) PHARMACEUTICAL
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=> d

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L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
AN 2000:531658 CAPLUS
DN 133:144896
TI Phosphonated agents and their antiangiogenic and antitumorigenic use
IN Collins, Delwood C.; Gagliardi, Antonio R.; Nickel, Peter
PA University of Kentucky Research Foundation, USA
SO U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 899,996, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2
```

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6096730	A	20000801	US 1998-121124	19980723
	US 6160166	A	20001212	US 1999-357925	19990721
PRAI	US 1997-899996	B2	19970724		
	US 1998-121124	A3	19980723		

```
OS MARPAT 133:144896
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
          ALL CITATIONS AVAILABLE IN THE RE FORMAT
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=> d hitstr

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L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
IT 5337-17-7, 4-Aminobenzenephosphonic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
    (prepn. and pharmaceutical compn. of antiangiogenic and
    antitumorigenic phosphonic acid agents)
RN 5337-17-7 CAPLUS
```

L5 1 S L4 AND (BLOOD OR TISSUE FACTOR OR TF OR THROMBOSIS)

=> s phosphonic acid and thrombosis

18832 PHOSPHONIC  
5 PHOSPHONICS  
18835 PHOSPHONIC  
(PHOSPHONIC OR PHOSPHONICS)  
3529172 ACID  
1349230 ACIDS  
3992609 ACID  
(ACID OR ACIDS)  
16601 PHOSPHONIC ACID  
(PHOSPHONIC(W)ACID)  
15745 THROMBOSIS

L6 4 PHOSPHONIC ACID AND THROMBOSIS

=> d ibib abs 1-4

L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:409274 CAPLUS

DOCUMENT NUMBER: 137:723

TITLE: Use of bisphosphonates for treatment or prophylaxis of undesired **thrombosis**

INVENTOR(S): Jiao, Jin-an; Luepschen, Lawrence K.; Nieves, Esperanza L.; Wong, Hing C.; Taylor, Dean P.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 29 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002065327	A1	20020530	US 1999-406269	19990924
PRIORITY APPLN. INFO.:			US 1999-406269	19990924

OTHER SOURCE(S): MARPAT 137:723

AB The invention discusses phosphonates, esp. bisphosphonates for treatment or prophylaxis of undesired **thrombosis**. The invention also discloses method of treatment as well as pharmaceutical compns. that utilize or comprise one or more of these compds.

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:208284 CAPLUS

DOCUMENT NUMBER: 134:252467

TITLE: Preparation of **phosphonic acid** derivatives having carboxypeptidase B inhibitory activity

INVENTOR(S): Fushihara, Kenichi; Kikuchi, Chika; Matsushima, Tetsuya; Kanemoto, Kenichi; Satoh, Eriko; Yamamoto, Takehiro; Suzuki, Kokichi

PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan

SOURCE: PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019836	A1	20010322	WO 2000-JP6248	20000913

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

*update STN Search Jan 2003*



CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

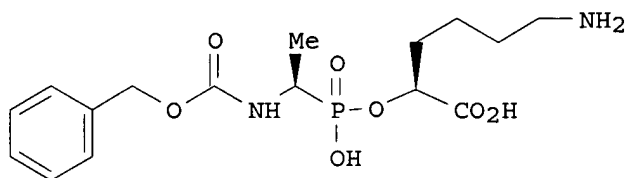
EP 1152004 A1 20011107 EP 2000-960970 20000913  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO

EP 1174434 A1 20020123 EP 2001-125712 20000913  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

BR 2000014615 A 20020618 BR 2000-14615 20000913  
JP 2002201196 A2 20020716 JP 2001-337503 20000913

PRIORITY APPLN. INFO.:  
JP 1999-260993 A 19990914  
JP 2000-84145 A 20000324  
EP 2000-960970 A3 20000913  
JP 2001-523413 A3 20000913  
WO 2000-JP6248 W 20000913

OTHER SOURCE(S): MARPAT 134:252467  
GI



I

AB Title compds. [R1CONHCR2R3P(O)(OH)XC(A)(E)CO2H; wherein R1 represents hydrogen, alkyl, substituted alkyl, etc.; R2 and R3 each represents hydrogen, alkyl, substituted alkyl, alkoxy, etc.; X represents CH2, O, or NH; A represents a group represented by formula (R7R8N(CR9R10)m) (wherein R7 and R8 each represents hydrogen, alkyl, acyl, alkoxycarbonyl, etc.; and R9 and R10 each represents hydrogen, halogeno, hydroxy, Ph, alkyl, etc.), etc.; E represents hydrogen, etc.] and pharmacol. acceptable salts are prepd. These compds. have carboxypeptidase B inhibitory activity and are useful for the treatment and/or prevention of thrombotic diseases in mammal. Thus, the title compd. I was prepd. and tested.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2000:323253 CAPLUS  
DOCUMENT NUMBER: 132:334655  
TITLE: preparation of himbacine analogs as thrombin receptor antagonists  
INVENTOR(S): Chackalamannil, Samuel; Asberom, Theodros; Xia, Yan; Doller, Dario; Clasby, Martin C.; Czarniecki, Michael F.  
PATENT ASSIGNEE(S): Schering Corp., USA  
SOURCE: U.S., 161 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1

ACCESSION NUMBER: 1995:223077 CAPLUS  
 DOCUMENT NUMBER: 122:96228  
 TITLE: Competitive N-methyl-D-aspartate receptor blockade reduces brain injury following transient focal ischemia in cats  
 AUTHOR(S): Nishikawa, Toshiaki; Kirsch, Jeffrey R.; Koehler, Raymond C.; Miyabe, Masayuki; Traystman, Richard J.  
 CORPORATE SOURCE: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD, 21287-4963, USA  
 SOURCE: Stroke (1994), 25(11), 2258-64  
 CODEN: SJCCA7; ISSN: 0039-2499  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB We tested the hypothesis that administration of the competitive N-methyl-D-aspartate (NMDA) receptor antagonist NPC 17742 (2R,4R,5S-[2-amino-4,5-(1,2-cyclohexyl)-7-phosphonoheptanoic acid]) during transient focal ischemia affects early postischemic brain injury. Halothane-anesthetized cats underwent 1 h of left middle cerebral artery occlusion plus 4 h of reperfusion. Control cats received saline (n=7). Exptl. cats were treated with NPC 17742 at a dose of 5 mg/kg IV from 45 min of ischemia to 15 min of reperfusion and 2.5 mg/kg per h for 4 h of reperfusion (NPC-5; n=7) or 50 mg/kg from 45 min of ischemia to 15 min of reperfusion and 25 mg/kg per h for 4 h of reperfusion (NPC-50; n=5). Microsphere-detd. **blood** flow to the ipsilateral inferior temporal cortex and caudate nucleus decreased to the same extent during ischemia and recovered to the same extent during reperfusion in the three groups. Triphenyltetrazolium-detd. injury vol. of ipsilateral cerebral hemisphere (saline, 24.+--.8%; NPC-5, 4.+--.2%; NPC-50, 5.+--.2% of hemisphere; mean.+--.SE) and caudate nucleus (saline, 72.+--.6%; NPC-5, 37.+--.10%; NPC-50, 26.+--.4%) was less in cats treated with both doses of drug compared with cats treated with saline. Recovery of somatosensory evoked potential amplitude was incomplete and similar in all groups (saline, 36.+--.14%; NPC-5, 58.+--.8%; NPC-50, 51.+--.15% of baseline). These data indicate that activation of NMDA receptors plays an important role in the mechanism of acute injury in both cortex and caudate after 1 h of transient focal ischemia in the cat. Because NPC 17742 afforded protection when administered at the end of ischemia and during reperfusion, NMDA receptor activation during reperfusion may contribute to the progression of injury in ischemic border regions.

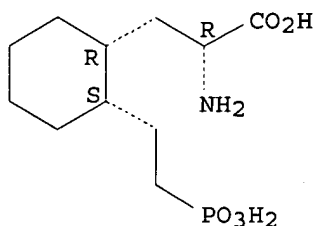
IT 144301-37-1, NPC 17742  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(competitive N-methyl-D-aspartate receptor blockade reduces brain injury following transient focal ischemia in cats)

RN 144301-37-1 CAPLUS

CN Cyclohexanepropanoic acid, .alpha.-amino-2-(2-phosphonoethyl)-, (.alpha.R,1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1995:223077 CAPLUS  
 DOCUMENT NUMBER: 122:96228  
 TITLE: Competitive N-methyl-D-aspartate receptor blockade reduces brain injury following transient focal ischemia in cats  
 AUTHOR(S): Nishikawa, Toshiaki; Kirsch, Jeffrey R.; Koehler, Raymond C.; Miyabe, Masayuki; Traystman, Richard J.  
 CORPORATE SOURCE: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD, 21287-4963, USA  
 SOURCE: Stroke (1994), 25(11), 2258-64  
 CODEN: SJCCA7; ISSN: 0039-2499  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB We tested the hypothesis that administration of the competitive N-methyl-D-aspartate (NMDA) receptor antagonist NPC 17742 (2R,4R,5S-[2-amino-4,5-(1,2-cyclohexyl)-7-phosphonoheptanoic acid]) during transient focal ischemia affects early postischemic brain injury. Halothane-anesthetized cats underwent 1 h of left middle cerebral artery occlusion plus 4 h of reperfusion. Control cats received saline (n=7). Exptl. cats were treated with NPC 17742 at a dose of 5 mg/kg IV from 45 min of ischemia to 15 min of reperfusion and 2.5 mg/kg per h for 4 h of reperfusion (NPC-5; n=7) or 50 mg/kg from 45 min of ischemia to 15 min of reperfusion and 25 mg/kg per h for 4 h of reperfusion (NPC-50; n=5). Microsphere-detd. blood flow to the ipsilateral inferior temporal cortex and caudate nucleus decreased to the same extent during ischemia and recovered to the same extent during reperfusion in the three groups. Triphenyltetrazolium-detd. injury vol. of ipsilateral cerebral hemisphere (saline, 24.+- .8%; NPC-5, 4.+- .2%; NPC-50, 5.+- .2% of hemisphere; mean.+- .SE) and caudate nucleus (saline, 72.+- .6%; NPC-5, 37.+- .10%; NPC-50, 26.+- .4%) was less in cats treated with both doses of drug compared with cats treated with saline. Recovery of somatosensory evoked potential amplitude was incomplete and similar in all groups (saline, 36.+- .14%; NPC-5, 58.+- .8%; NPC-50, 51.+- .15% of baseline). These data indicate that activation of NMDA receptors plays an important role in the mechanism of acute injury in both cortex and caudate after 1 h of transient focal ischemia in the cat. Because NPC 17742 afforded protection when administered at the end of ischemia and during reperfusion, NMDA receptor activation during reperfusion may contribute to the progression of injury in ischemic border regions.

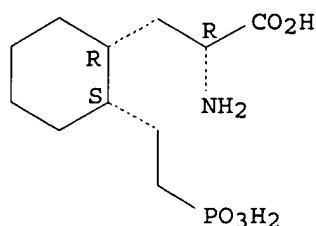
IT 144301-37-1, NPC 17742  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(competitive N-methyl-D-aspartate receptor blockade reduces brain injury following transient focal ischemia in cats)

RN 144301-37-1 CAPLUS

CN Cyclohexanepropanoic acid, .alpha.-amino-2-(2-phosphonoethyl)-, (.alpha.R,1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6063847	A	20000516	US 1998-197442	19981123
US 6326380	B1	20011204	US 2000-545720	20000407
PRIORITY APPLN. INFO.:			US 1997-66518P	P 19971125
			US 1998-197442	A3 19981123

OTHER SOURCE(S):           MARPAT 132:334655  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Heterocyclic-substituted tricyclics of the formula (I) [single dotted line represents an optional double bond; double dotted line represents an optional single bond; n = 0-2; Q = (un)substituted cycloalkyl, heterocycloalkyl, aryl or heteroaryl; Het = (un)substituted mono-, bi- or tricyclic heteroarom. group; B = -(CH<sub>2</sub>)<sub>n3</sub>-, wherein n<sub>3</sub> is 0-5, -CH<sub>2</sub>-O-, -CH<sub>2</sub>S-, -CH<sub>2</sub>-NR<sub>6</sub>-, -C(O)NR<sub>6</sub>-, -NR<sub>6</sub>C(O)-, etc.; X = -O- or -NR<sub>6</sub>- when the double dotted line represents a single bond, or X is -OH or -NHR<sub>20</sub> when the bond is absent; Y = =O, =S, (H, H), (H, OH) or (H, alkoxy) when the double dotted line represents a single bond, or when the bond is absent, Y = O, (H, H), (H, OH), (H, SH) or (H, C<sub>1</sub>-C<sub>6</sub> alkoxy); R<sub>15</sub> is absent when the double dotted line represents a single bond and is H, -NR<sub>18</sub>R<sub>19</sub>, or -OR<sub>17</sub> when the bond is absent; or Y = -O-(CH<sub>2</sub>)<sub>m</sub>-O- or -S-(CH<sub>2</sub>)<sub>m</sub>-S-, m = 1-2; and R<sub>15</sub>, R<sub>17</sub>, R<sub>18</sub>, R<sub>19</sub> = H or alkyl, aryl etc.] or a pharmaceutically acceptable salt were synthesized. Thus (II) was prepd. starting from (R)-3-butyn-2-ol and via condensation of fragment (III) and [5-[3-(trifluoromethyl)phenyl]-2-pyridinyl]methyl-**phosphonic acid** di-Et ester. II shows an IC<sub>50</sub> of 0.11 nM in in vitro thrombin receptor antagonist assay. Phamaceutical compns. contg. I as well as method of treating diseases assocd. with **thrombosis**, atherosclerosis, restenosis, hypertension, angina pectoris, arrhythmia, heart failure, and cancer are described.

REFERENCE COUNT:           11       THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:           1999:59284 CAPLUS

DOCUMENT NUMBER:           130:246279

TITLE:                      Antagonists of the Platelet P2T Receptor: A Novel Approach to Antithrombotic Therapy

AUTHOR(S):                  Ingall, Anthony H.; Dixon, John; Bailey, Andrew; Coombs, Mandy E.; Cox, David; McInally, Judith I.; Hunt, Simon F.; Kindon, Nicholas D.; Teobald, Barry J.; Willis, Paul A.; Humphries, Robert G.; Leff, Paul; Clegg, Jane A.; Smith, James A.; Tomlinson, Wendy

CORPORATE SOURCE:           Departments of Medicinal Chemistry and Pharmacology, ASTRA Charnwood, Loughborough, LE11 5RH, UK

SOURCE:                    Journal of Medicinal Chemistry (1999), 42(2), 213-220  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:                  American Chemical Society

DOCUMENT TYPE:              Journal

LANGUAGE:                   English

AB The platelet P2T receptor plays a major role in platelet aggregation, and its antagonists are predicted to have significant therapeutic potential as antithrombotic agents. We have explored analogs of ATP, which is a weak, nonselective but competitive P2T receptor antagonist. Modification of the polyphosphate side chain to prevent breakdown to the agonist ADP and substitution of the adenine moiety to enhance affinity and selectivity for the P2T receptor led to the identification of compd. AR-C67085MX, having

an IC50 of 2.5 nM against ADP-induced aggregation of human platelets. This compd. was the first very potent antagonist of the P2T receptor, with a selectivity for that subtype of the P2 receptor family of >1000-fold. Further modification of the structure produced compd. AR-C69931MX having an IC50 of 0.4 nM. In vivo, at maximally effective antithrombotic doses, there is little prolongation of bleeding time (1.4-fold), which is in marked contrast to the 5-6-fold found with GPIIb/IIIa antagonists.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

IT Purinoceptors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(P2T; prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

IT Anticoagulants

(prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

IT Structure-activity relationship

(receptor-inhibiting; prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

IT Structure-activity relationship

(**thrombosis**-inhibiting; prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

IT 81336-74-5P, 5'-Adenylic acid, monoanhydride with (dichloromethylene)bis[**phosphonic acid**] 81336-78-9P 145783-24-0P

145783-27-3P 163706-06-7P 163706-10-3P 163706-13-6P 163706-15-8P

163706-18-1P 163706-19-2P 164992-25-0P 221552-87-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

IT 16321-99-6 43157-50-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

IT 145783-19-3P 163706-51-2P 163706-52-3P 163706-56-7P 163706-58-9P

163706-59-0P 221552-84-7P 221552-85-8P 221552-86-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and structure of platelet P2T receptor antagonists as novel approach to antithrombotic therapy)

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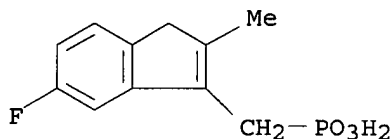
E1 THROUGH E443 ASSIGNED

ACCESSION NUMBER: 1974:505092 CAPLUS  
 DOCUMENT NUMBER: 81:105092  
 TITLE: 5-Fluoro-2-methyl-1-indenylidene compounds  
 INVENTOR(S): Shen, Tsung-Ying; Jones, Howard  
 PATENT ASSIGNEE(S): Merck and Co., Inc.  
 SOURCE: Ger. Offen., 35 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2360550	A1	19740612	DE 1973-2360550	19731205
US 3860636	A	19750114	US 1972-312549	19721206
GB 1418950	A	19751224	GB 1973-55832	19731203
FR 2209562	B1	19781110	FR 1973-43196	19731204
JP 49086353	A2	19740819	JP 1973-135794	19731206
CH 613688	A	19791015	CH 1973-17113	19731206
			US 1972-312549	19721206

PRIORITY APPLN. INFO.:

GI For diagram(s), see printed CA Issue.  
 AB Eight indenenes [I, n = 0 or 1; R = 5-tetrazolyl, 2-(5-tetrazolyl)ethyl, CH<sub>2</sub>SO<sub>3</sub>H, or CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>; R<sub>1</sub> = H or Cl; Z = O, CH:CH, or C.tplbond.C], useful as analgesics, antipyretics, and **inflammation** inhibitors (no data), were prepd. by reaction of 3-R-substituted 5-fluoro-2-methylindenenes with 3,4-R<sub>1</sub>(MeSO<sub>n</sub>)C<sub>6</sub>H<sub>3</sub>ZCHO.  
 IT **53533-20-3P**  
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)  
 RN 53533-20-3 CAPLUS  
 CN Phosphonic acid, [(5-fluoro-2-methyl-1H-inden-3-yl)methyl]- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1974:505092 CAPLUS  
 DOCUMENT NUMBER: 81:105092  
 TITLE: 5-Fluoro-2-methyl-1-indenylidene compounds  
 INVENTOR(S): Shen, Tsung-Ying; Jones, Howard  
 PATENT ASSIGNEE(S): Merck and Co., Inc.  
 SOURCE: Ger. Offen., 35 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2360550	A1	19740612	DE 1973-2360550	19731205
US 3860636	A	19750114	US 1972-312549	19721206
GB 1418950	A	19751224	GB 1973-55832	19731203
FR 2209562	B1	19781110	FR 1973-43196	19731204
JP 49086353	A2	19740819	JP 1973-135794	19731206
CH 613688	A	19791015	CH 1973-17113	19731206
			US 1972-312549	19721206

PRIORITY APPLN. INFO.:

GI For diagram(s), see printed CA Issue.

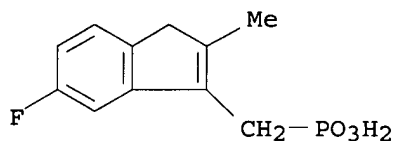
AB Eight indenenes [I, n = 0 or 1; R = 5-tetrazolyl, 2-(5-tetrazolyl)ethyl, CH<sub>2</sub>SO<sub>3</sub>H, or CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>; R<sub>1</sub> = H or Cl; Z = O, CH:CH, or C.tplbond.C], useful as analgesics, antipyretics, and **inflammation** inhibitors (no data), were prepd. by reaction of 3-R-substituted 5-fluoro-2-methylindenenes with 3,4-R<sub>1</sub>(MeSO<sub>n</sub>)C<sub>6</sub>H<sub>3</sub>ZCHO.

IT 53533-20-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 53533-20-3 CAPLUS

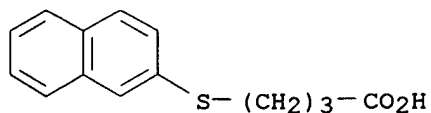
CN Phosphonic acid, [(5-fluoro-2-methyl-1H-inden-3-yl)methyl]- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1995:967540 CAPLUS  
 DOCUMENT NUMBER: 124:45717  
 TITLE: Preparation of naphthalene derivatives as tissue thromboplastin inhibitors and **pharmaceuticals** containing them  
 INVENTOR(S): Takenochi, Kazuya; Horiuchi, Hideki; Hasegawa, Masakazu; Takeuchi, Takahiro; Komorya, Keiji  
 PATENT ASSIGNEE(S): Teijin Ltd, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07242538	A2	19950919	JP 1994-34684	19940304

OTHER SOURCE(S): MARPAT 124:45717  
 GI For diagram(s), see printed CA Issue.  
 AB Prophylactic or therapeutic agents, which inhibit **tissue factor** (TF), contg. naphthalene derivs. I (A = CH<sub>2</sub>CH<sub>2</sub>, CH:CH, C.tplbond.C, SCH<sub>2</sub>, OCH<sub>2</sub>; B = CH<sub>2</sub>CH<sub>2</sub>, CH:CH; R = H, C1-4 alkyl; n = 0-5)  
 or  
 their **pharmaceutically** acceptable salts as active ingredients are claimed. The agents useful for DIC (disseminated intravascular coagulation), thrombosis, intimal thickening diseases, or postoperative opacification of the lens in cataract patients are also claimed.  
 2-[7-(2-Naphthylthio)heptanamido]benzoic acid (II, prepn. given) at 3 .mu.M suppressed TF formation by human peripheral blood mononuclear leukocyte at inhibition rate 79.0%. Tablets contg. II were also formulated.  
 IT 5324-80-1, 4-(2-Naphthylthio)butanoic acid 85388-18-7  
 109397-47-9, 7-(2-Naphthyl)heptanoic acid 156387-68-7,  
 8-(2-Naphthyl)octanoic acid 172087-30-8, 7-(2-Naphthylthio)heptanoic acid 172087-31-9, 5-(2-Naphthylthio)pentanoic acid 172087-32-0, 6-(2-Naphthylthio)hexanoic acid 172087-33-1 172087-34-2  
 172087-35-3 172087-36-4 172087-37-5  
 172087-38-6 172087-39-7 172087-40-0  
 172087-41-1  
 RL: RCT (Reactant)  
 (amidation with Me anthranilate; **tissue factor inhibitors** contg. [naphthyl(oxy or thio)alkanamido]benzoic acids)  
 RN 5324-80-1 CAPLUS  
 CN Butanoic acid, 4-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

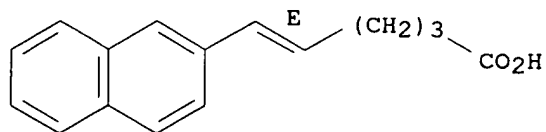




RN 85388-18-7 CAPLUS

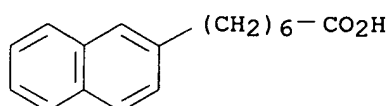
CN 5-Hexenoic acid, 6-(2-naphthalenyl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



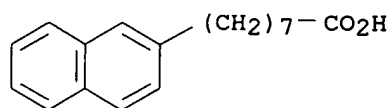
RN 109397-47-9 CAPLUS

CN 2-Naphthaleneheptanoic acid (6CI, 9CI) (CA INDEX NAME)



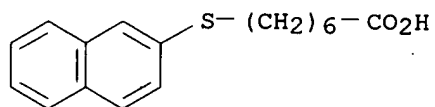
RN 156387-68-7 CAPLUS

CN 2-Naphthaleneoctanoic acid (9CI) (CA INDEX NAME)



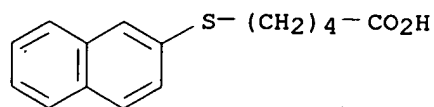
RN 172087-30-8 CAPLUS

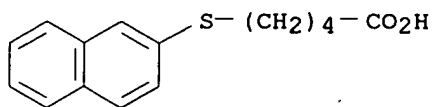
CN Heptanoic acid, 7-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



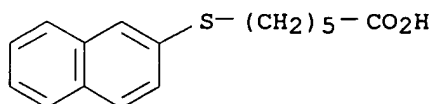
RN 172087-31-9 CAPLUS

CN Pentanoic acid, 5-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

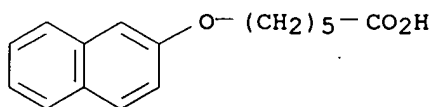




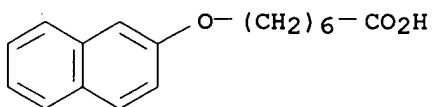
RN 172087-32-0 CAPLUS  
 CN Hexanoic acid, 6-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)



RN 172087-33-1 CAPLUS  
 CN Hexanoic acid, 6-(2-naphthalenyloxy)- (9CI) (CA INDEX NAME)

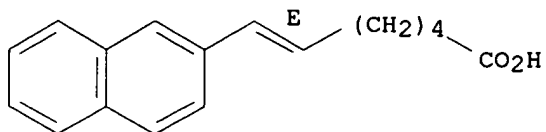


RN 172087-34-2 CAPLUS  
 CN Heptanoic acid, 7-(2-naphthalenyloxy)- (9CI) (CA INDEX NAME)



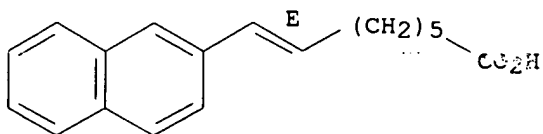
RN 172087-35-3 CAPLUS  
 CN 6-Heptenoic acid, 7-(2-naphthalenyl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 172087-36-4 CAPLUS  
 CN 7-Octenoic acid, 8-(2-naphthalenyl)-, (E)- (9CI) (CA INDEX NAME)

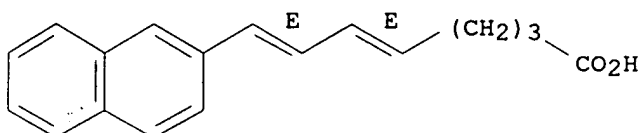
Double bond geometry as shown.



RN 172087-37-5 CAPLUS

CN 5,7-Octadienoic acid, 8-(2-naphthalenyl)-, (E,E)- (9CI) (CA INDEX NAME)

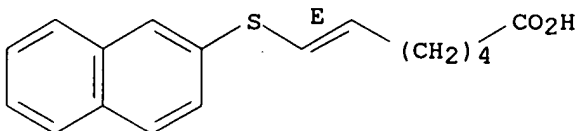
Double bond geometry as shown.



RN 172087-38-6 CAPLUS

CN 6-Heptenoic acid, 7-(2-naphthalenylthio)-, (E)- (9CI) (CA INDEX NAME)

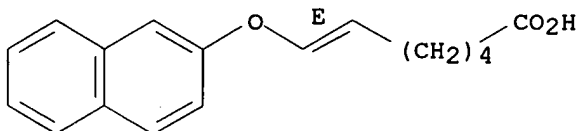
Double bond geometry as shown.



RN 172087-39-7 CAPLUS

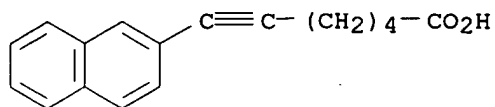
CN 6-Heptenoic acid, 7-(2-naphthalenyloxy)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

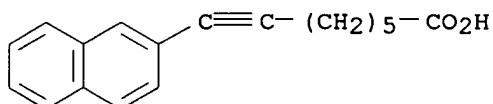


RN 172087-40-0 CAPLUS

CN 6-Heptynoic acid, 7-(2-naphthalenyl)- (9CI) (CA INDEX NAME)



RN 172087-41-1 CAPLUS  
 CN 7-Octynoic acid, 8-(2-naphthalenyl)- (9CI) (CA INDEX NAME)



IT 169238-43-1P 172086-94-1P 172086-95-2P  
 172086-96-3P 172086-97-4P 172086-98-5P  
 172086-99-6P 172087-00-2P 172087-01-3P  
 172087-02-4P 172087-03-5P 172087-04-6P  
 172087-05-7P 172087-06-8P 172087-07-9P  
 172087-08-0P 172087-09-1P 172087-10-4P  
 172087-11-5P 172087-12-6P 172087-13-7P  
 172087-14-8P 172087-15-9P 172087-16-0P  
 172087-17-1P 172087-18-2P 172087-19-3P  
 172087-20-6P 172087-21-7P 172087-22-8P  
 172087-23-9P 172087-24-0P 172087-25-1P  
 172087-26-2P 172087-27-3P 172087-29-5P

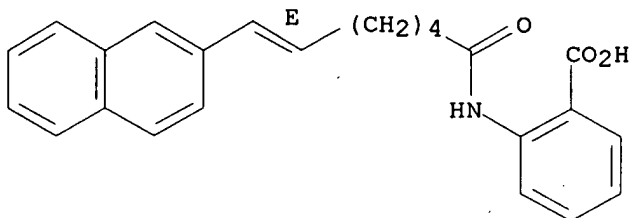
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(tissue factor inhibitors contg.

[naphthyl(oxy or thio)alkanamido]benzoic acids)

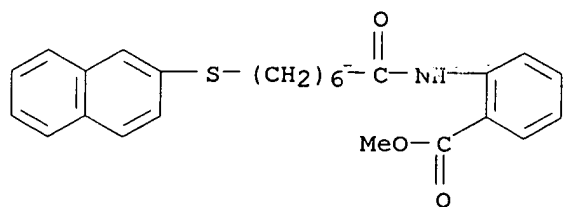
RN 169238-43-1 CAPLUS  
 CN Benzoic acid, 2-[[[(6E)-7-(2-naphthalenyl)-1-oxo-6-heptenyl]amino]- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



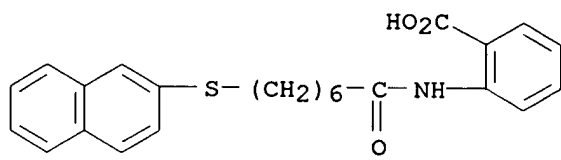
RN 172086-94-1 CAPLUS  
 CN Benzoic acid, 2-[[[7-(2-naphthalenylthio)-1-oxoheptyl]amino]-, methyl ester

(9CI) (CA INDEX NAME)



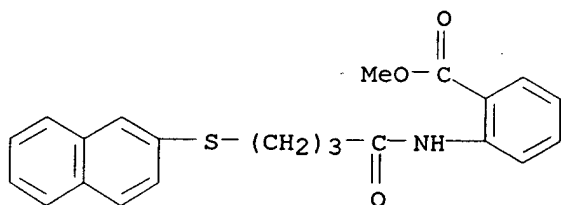
RN 172086-95-2 CAPLUS

CN Benzoic acid, 2-[[7-(2-naphthalenylthio)-1-oxoheptyl]amino]- (9CI) (CA INDEX NAME)



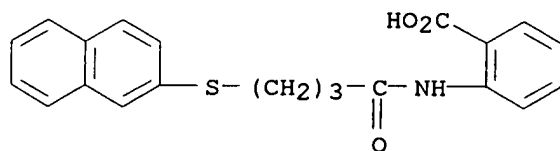
RN 172086-96-3 CAPLUS

CN Benzoic acid, 2-[[4-(2-naphthalenylthio)-1-oxobutyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



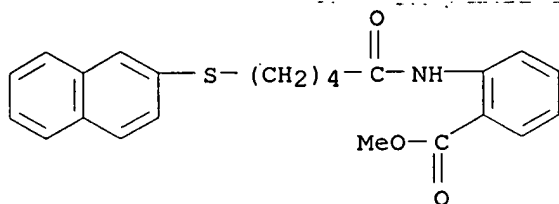
RN 172086-97-4 CAPLUS

CN Benzoic acid, 2-[[4-(2-naphthalenylthio)-1-oxobutyl]amino]- (9CI) (CA INDEX NAME)

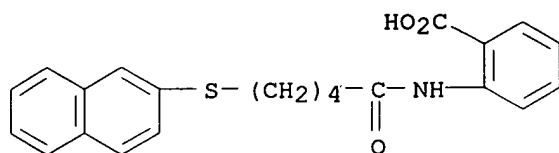


RN 172086-98-5 CAPLUS

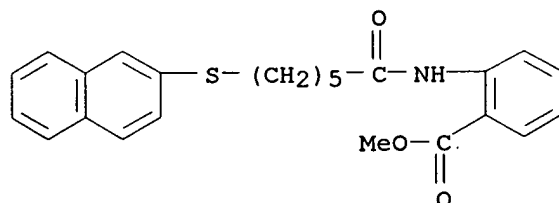
CN Benzoic acid, 2-[[5-(2-naphthalenylthio)-1-oxopentyl]amino]-, methyl ester  
(9CI) (CA INDEX NAME)



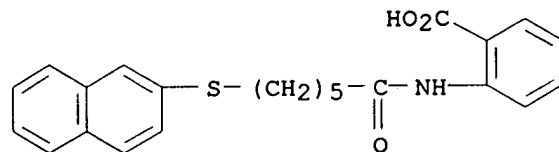
RN 172086-99-6 CAPLUS  
CN Benzoic acid, 2-[[5-(2-naphthalenylthio)-1-oxopentyl]amino]- (9CI) (CA INDEX NAME)



RN 172087-00-2 CAPLUS  
CN Benzoic acid, 2-[[6-(2-naphthalenylthio)-1-oxohexyl]amino]-, methyl ester  
(9CI) (CA INDEX NAME)

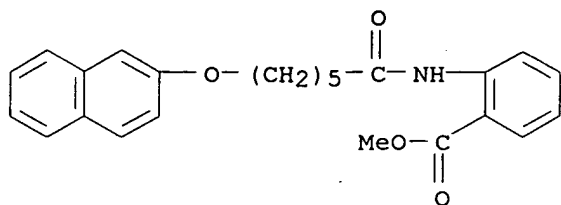


RN 172087-01-3 CAPLUS  
CN Benzoic acid, 2-[[6-(2-naphthalenylthio)-1-oxohexyl]amino]- (9CI) (CA INDEX NAME)



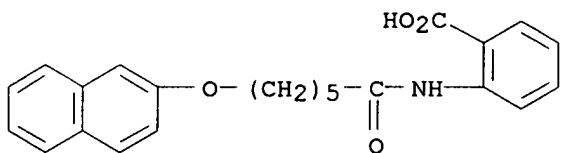
RN 172087-02-4 CAPLUS

CN Benzoic acid, 2-[[6-(2-naphthalenyloxy)-1-oxohexyl]amino]-, methyl ester  
(9CI) (CA INDEX NAME)



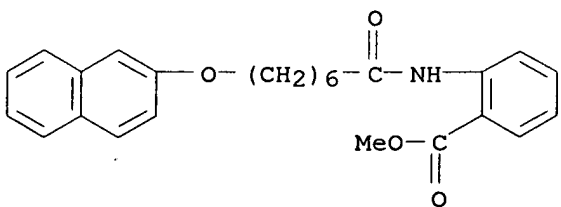
RN 172087-03-5 CAPLUS

CN Benzoic acid, 2-[[6-(2-naphthalenyloxy)-1-oxohexyl]amino]- (9CI) (CA INDEX NAME)



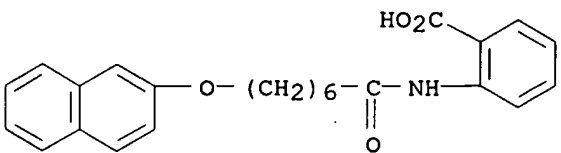
RN 172087-04-6 CAPLUS

CN Benzoic acid, 2-[[7-(2-naphthalenyloxy)-1-oxoheptyl]amino]-, methyl ester  
(9CI) (CA INDEX NAME)

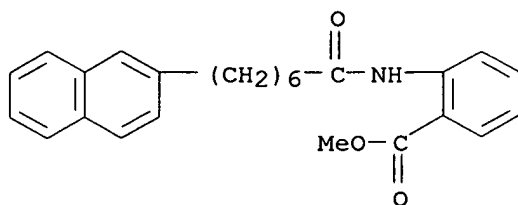


RN 172087-05-7 CAPLUS

CN Benzoic acid, 2-[[7-(2-naphthalenyloxy)-1-oxoheptyl]amino]- (9CI) (CA INDEX NAME)

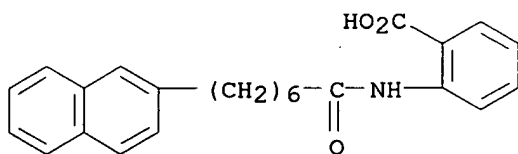


RN 172087-06-8 CAPLUS

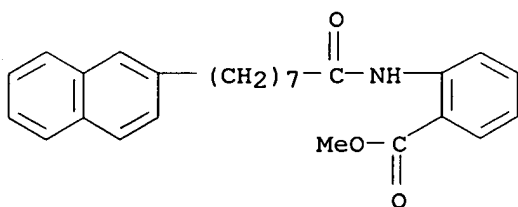
CN Benzoic acid, 2-[[7-(2-naphthalenyl)-1-oxoheptyl]amino]-, methyl ester  
(9CI) (CA INDEX NAME)

RN 172087-07-9 CAPLUS

CN Benzoic acid, 2-[[7-(2-naphthalenyl)-1-oxoheptyl]amino]- (9CI) (CA INDEX NAME)

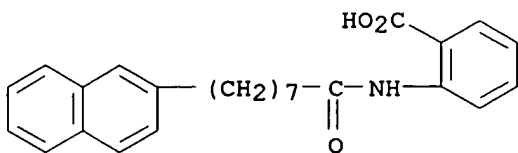


RN 172087-08-0 CAPLUS

CN Benzoic acid, 2-[[8-(2-naphthalenyl)-1-oxooctyl]amino]-, methyl ester  
(9CI) (CA INDEX NAME)

RN 172087-09-1 CAPLUS

CN Benzoic acid, 2-[[8-(2-naphthalenyl)-1-oxooctyl]amino]- (9CI) (CA INDEX NAME)





ACCESSION NUMBER: 1996:541311 CAPLUS  
 DOCUMENT NUMBER: 125:212249  
 TITLE: Anticoagulant effects and **tissue factor** pathway inhibitor after intrapulmonary low-molecular-weight heparin  
 AUTHOR(S): ~~Harenberg, J.; Malsch, R.; Angelescu, M.; Lange, C.; Michaelis, H-C.; Wolf, H.; Heene, D. L.~~  
 CORPORATE SOURCE: 1st Dep. Med., Univ. Heidelberg, Mannheim, 68167, Germany  
 SOURCE: Blood Coagulation Fibrinolysis (1996), 7(4), 477-483  
 CODEN: BLFIE7; ISSN: 0957-5235  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The present study was designed to investigate the anticoagulant action of inhaled low-mol.-wt. (LMW) heparin on the release of **tissue factor** pathway inhibitor (TFPI) and on antifactor Xa activity, Heptest, activated partial thromboplastin time (APTT) and thrombin clotting

time (TCT) in healthy volunteers. 3000 IU (group 1), 9000 IU (group 2), 27000 IU (group 3) or 54000 IU (group 4) LMW-heparin were given to 20 healthy volunteers each at 4 wk intervals by inhalation. For safety reasons a dose escalating design was chosen. APTT and TCT did not change after inhalation of any dose of LMW-heparin as well as all parameters in group 1. In group 2, Heptest coagulation times were prolonged from 18.7+-.2.0 s before to 26.1+-.5.2 s 6 h and 20.5+-.1.9 s 24 h after inhalation and the other parameters remained unaffected. In group 3, S2222 method and the protamine assay increased from 0.01 to about 0.1 IU/mL 6 h after inhalation and returned to normal values after 24 h.

TFPI antigen increased from 74.1+-.13.9 to 80.5+-.14.2 ng/mL 3 h after inhalation. TFPI activity remained unchanged. Heptest coagulation

values were prolonged to 42.+-.7.6 s after 6 h and returned to normal within 72

h after inhalation. In group 4, the following changes were obsd.: antifactor Xa activity increased to 0.343+-.0.196 U/mL after 6 h and normalized after 72 h. The protamine assay detected 0.2.+-.0.18 U

LMWH/mL after 6 h, TFPI antigen increased to 103.+-.17.9 ng/mL and TFPI activity to 1.14.+-.0.23 U 3 h after inhalation. All tests were normal after 24

h. Heptest coagulation values increased to 77.5+-.11.8 s 6 h after inhalation and normalized after 144 h. The area under the activity time curve of the S2222 method and of the Heptest assay increased with increasing doses ( $r = 0.677$  and  $r = 0.571$ ), resp. The calcd. elimination half-life of the aXa-effect was 7.5 h using S2222-, Heptest- and

protamine assays. The data demonstrate a resorption of LMW-heparin by intrapulmonary route in man. The dose to produce antifactor Xa levels, prolongations of Heptest coagulation values and in releasing TFPI is

about ten-fold higher than after s.c. administration.

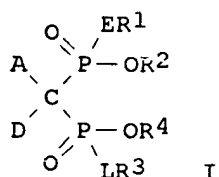
IT Anticoagulants and Antithrombotics  
 (antithrombotic and antiasthmatic effects, release of **tissue factor** pathway inhibitor and antifactor Xa activity after

- intrapulmonary low-mol.-wt. heparin)
- IT Blood-coagulation factors  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (LACI (lipoprotein-assocd. coagulation inhibitor), antithrombotic and  
 antiasthmatic effects, release of **tissue factor**  
 pathway inhibitor and antifactor Xa activity after intrapulmonary  
 low-mol.-wt. heparin)
- IT Bronchodilators  
 (antiasthmatics, antithrombotic and antiasthmatic effects, release of  
**tissue factor** pathway inhibitor and antifactor Xa  
 activity after intrapulmonary low-mol.-wt. heparin)
- IT Pharmaceutical dosage forms  
 (inhalants, antithrombotic and antiasthmatic effects, release of  
**tissue factor** pathway inhibitor and antifactor Xa  
 activity after intrapulmonary low-mol.-wt. heparin)
- IT 9002-05-5, Factor Xa  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (anti-; antithrombotic and antiasthmatic effects, release of  
**tissue factor** pathway inhibitor and antifactor Xa  
 activity after intrapulmonary low-mol.-wt. heparin)
- IT 9005-49-6, Heparin, biological studies  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antithrombotic and antiasthmatic effects, release of **tissue**  
**factor** pathway inhibitor and antifactor Xa activity after  
 intrapulmonary low-mol.-wt. heparin)

ACCESSION NUMBER: 1999:162340 CAPLUS  
 DOCUMENT NUMBER: 130:209820  
 TITLE: Substituted 1,1-bisphosphonates for use as enzyme inhibitors and drugs  
 INVENTOR(S): Brands, Michael; Lohrmann, Emanuel; Schmidt, Delf; Kirsten, Rolf; Riebel, Hans-Joachim; Eckenberg, Peter;  
 Hansen, Jutta; Raddatz, Siegfried; Schulze, Thomas; Trappe, Joerg  
 PATENT ASSIGNEE(S): Bayer A.-G., Germany  
 SOURCE: Ger. Offen., 68 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19738005	A1	19990304	DE 1997-19738005	19970830

OTHER SOURCE(S): MARPAT 130:209820  
 GI



AB Substituted 1,1-bisphosphonates [I; R1-R4 = H, C1-5 alkyl; A = (CO)a(CH2)bNR5R6, CH2ScR7, C(S)NHR8; D = H; or AD = :O, :CHR11, :NR12; R5 = H, C1-6 alkyl; R6 = H, C1-5 alkyl, cycloalkyl, (substituted) aryl, heteroaryl, etc.; R7, R8 = C3-7 cycloalkyl, (substituted) aryl, heteroaryl, etc.; R11, R12 = 2-fluorenyl, 4-benzyloxyphenyl, 9-phenanthryl, 2-thiazolyl, etc.; E, L = O, S; a, b, c = 0, 1] and their salts, enantiomers, and diastereomers are prepd. which (a) inhibit protein phosphatase 1 and are useful for treatment of cardiovascular disorders, and/or (b) inhibit HIV integrase and are useful for prevention and treatment of retroviral infections (no data). I are prepd. (a) by addn. reaction of tetra-Et vinylidene-1,1-bisphosphonate with appropriate thiols or amines, (b) by condensation of tetra-Et methylenebisphosphonate with appropriate bromomethyl compds., isocyanates, or aldehydes, or (c) by reaction of phosphite esters with appropriate amines and orthoformates or with R12N:CCl2. Thus, cyclohexanethiol reacted with di-Et [1-(diethoxyphosphino)vinyl]phosphonate to form di-Et [2-(cyclohexylthio)-1-(diethoxyphosphino)ethyl]phosphonate, which was converted to the free acid with BrSiMe3.

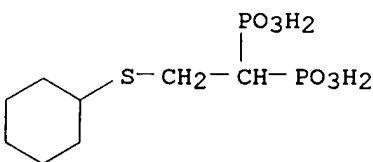
IT 221002-47-7P 221002-50-2P 221002-55-7P  
 221002-58-0P 221002-60-4P 221002-62-6P  
 221002-65-9P 221002-68-2P 221002-71-7P  
 221002-77-3P 221002-80-8P 221002-83-1P  
 221002-87-5P 221002-90-0P 221002-93-3P  
 221002-93-6P 221002-98-0P 221002-99-9P  
 221003-01-6P 221003-02-7P 221003-03-8P  
 221003-05-0P 221003-06-1P 221003-08-3P  
 221003-09-4P 221003-10-7P 221003-11-8P  
 221003-13-0P 221003-14-1P 221003-16-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(substituted bisphosphonates for use as enzyme inhibitors and drugs)

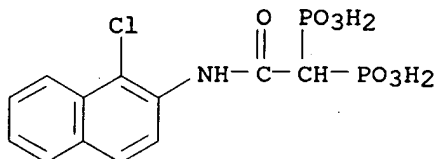
RN 221002-47-7 CAPLUS

CN Phosphonic acid, [2-(cyclohexylthio)ethylidene]bis- (9CI) (CA INDEX NAME)



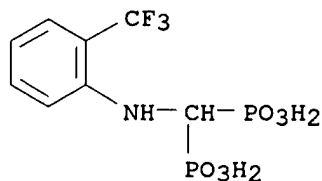
RN 221002-50-2 CAPLUS

CN Phosphonic acid, [2-[(1-chloro-2-naphthalenyl)amino]-2-oxoethylidene]bis- (9CI) (CA INDEX NAME)



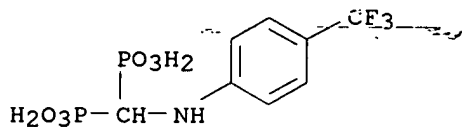
RN 221002-55-7 CAPLUS

CN Phosphonic acid, [[2-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI) (CA INDEX NAME)



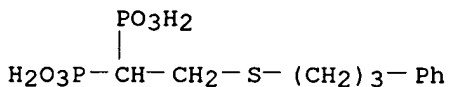
RN 221002-58-0 CAPLUS

CN Phosphonic acid, [[[4-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI)  
(CA INDEX NAME)



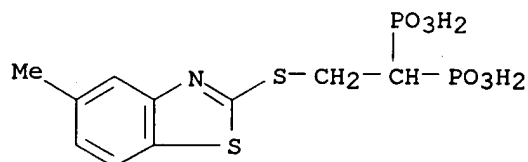
RN 221002-60-4 CAPLUS

CN Phosphonic acid, [2-[(3-phenylpropyl)thio]ethylidene]bis- (9CI) (CA  
INDEX  
NAME)



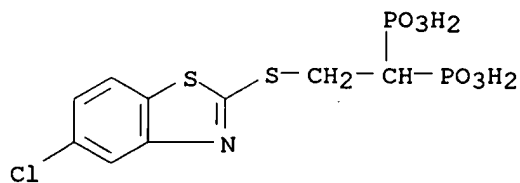
RN 221002-62-6 CAPLUS

CN Phosphonic acid, [2-[(5-methyl-2-benzothiazolyl)thio]ethylidene]bis-  
(9CI)  
(CA INDEX NAME)



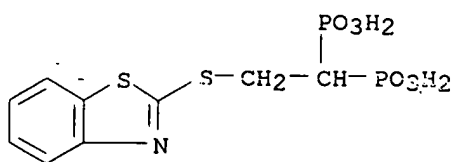
RN 221002-65-9 CAPLUS

CN Phosphonic acid, [2-[(5-chloro-2-benzothiazolyl)thio]ethylidene]bis-  
(9CI)  
(CA INDEX NAME)

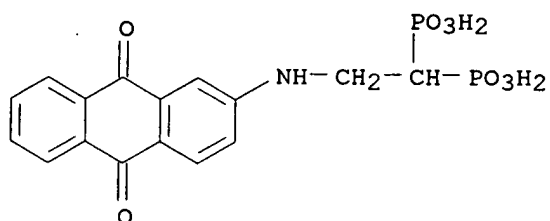


RN 221002-68-2 CAPLUS

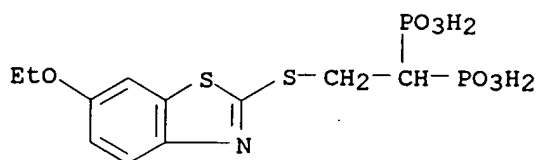
CN Phosphonic acid, [2-(2-benzothiazolylthio)ethylidene]bis- (9CI) (CA  
INDEX  
NAME)



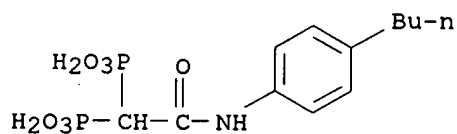
RN 221002-71-7 CAPLUS  
 CN Phosphonic acid, [2-[(9,10-dihydro-9,10-dioxo-2-anthracenyl)amino]ethylidene]bis- (9CI) (CA INDEX NAME)



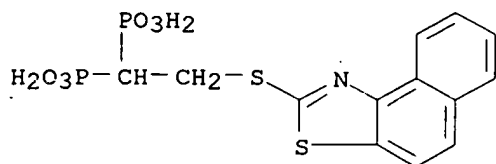
RN 221002-77-3 CAPLUS  
 CN Phosphonic acid, [2-[(6-ethoxy-2-benzothiazolyl)thio]ethylidene]bis- (9CI)  
 (CA INDEX NAME)



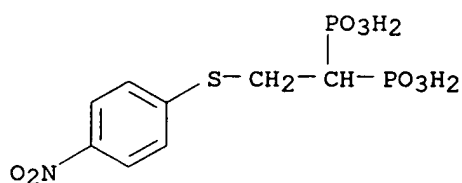
RN 221002-80-8 CAPLUS  
 CN Phosphonic acid, [2-[(4-butylphenyl)amino]-2-oxoethylidene]bis- (9CI)  
 (CA INDEX NAME)



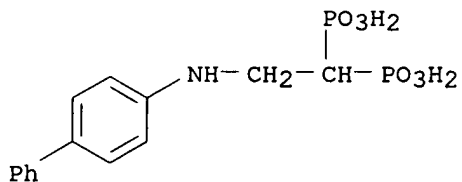
RN 221002-83-1 CAPLUS  
 CN Phosphonic acid, [2-(naphtho[1,2-d]thiazol-2-ylthio)ethylidene]bis- (9CI)  
 (CA INDEX NAME)



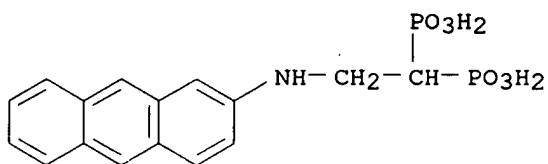
RN 221002-87-5 CAPLUS  
 CN Phosphonic acid, [2-[(4-nitrophenyl)thio]ethylidene]bis- (9CI) (CA INDEX NAME)



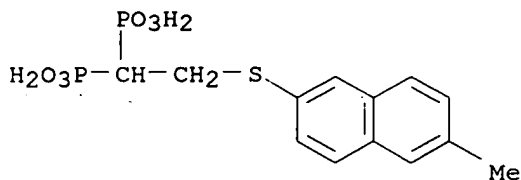
RN 221002-90-0 CAPLUS  
 CN Phosphonic acid, [2-([1,1'-biphenyl]-4-ylamino)ethylidene]bis- (9CI) (CA INDEX NAME)



RN 221002-93-3 CAPLUS  
 CN Phosphonic acid, [2-(2-anthracenylamino)ethylidene]bis- (9CI) (CA INDEX NAME)

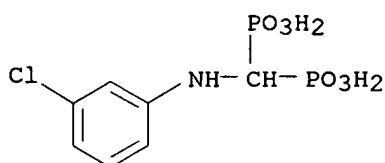


RN 221002-96-6 CAPLUS  
 CN Phosphonic acid, [2-[(6-methyl-2-naphthalenyl)thio]ethylidene]bis- (9CI) (CA INDEX NAME)



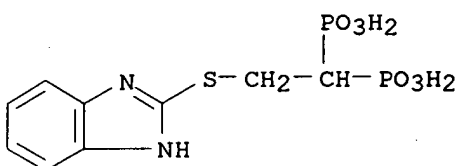
RN 221002-98-8 CAPLUS

CN Phosphonic acid, [[[3-chlorophenyl]amino]methylene]bis- (9CI) (CA INDEX NAME)



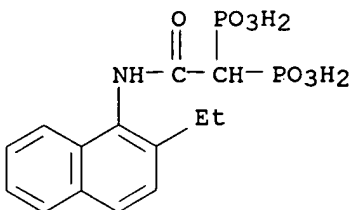
RN 221002-99-9 CAPLUS

CN Phosphonic acid, [2-(1H-benzimidazol-2-ylthio)ethylidene]bis- (9CI) (CA INDEX NAME)



RN 221003-01-6 CAPLUS

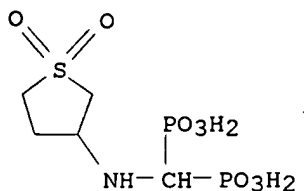
CN Phosphonic acid, [2-[(2-ethyl-1-naphthalenyl)amino]-2-oxoethylidene]bis- (9CI) (CA INDEX NAME)



RN 221003-02-7 CAPLUS

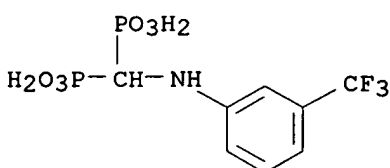
CN Phosphonic acid, [[[tetrahydro-1,1-dioxido-3-thienyl]amino]methylene]bis- (9CI) (CA INDEX NAME)





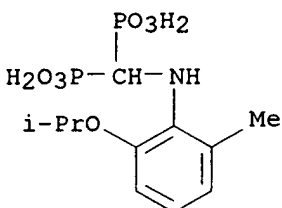
RN 221003-03-8 CAPLUS

CN Phosphonic acid, [[[3-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI)  
(CA INDEX NAME)



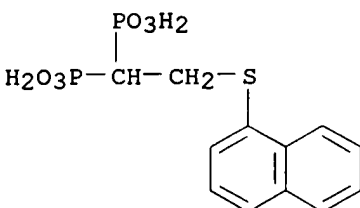
RN 221003-05-0 CAPLUS

CN Phosphonic acid,  
[[[2-methyl-6-(1-methylethoxy)phenyl]amino]methylene]bis-  
(9CI) (CA INDEX NAME)



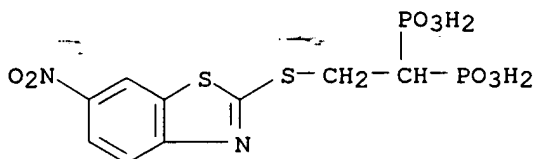
RN 221003-06-1 CAPLUS

CN Phosphonic acid, [2-(1-naphthalenylthio)ethylidene]bis- (9CI) (CA INDEX  
NAME)



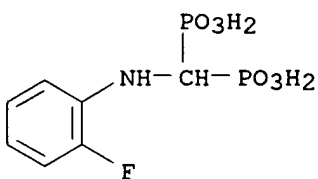
RN 221003-08-3 CAPLUS

CN Phosphonic acid, [2-[(6-nitro-2-benzothiazolyl)thio]ethylidene]bis- (9CI)  
(CA INDEX NAME)



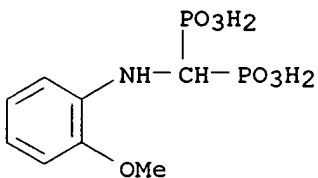
RN 221003-09-4 CAPLUS

CN Phosphonic acid, [[(2-fluorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



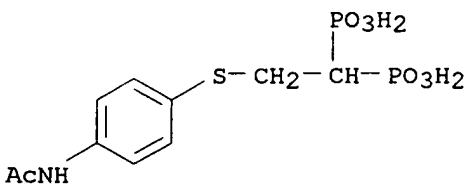
RN 221003-10-7 CAPLUS

CN Phosphonic acid, [[(2-methoxyphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



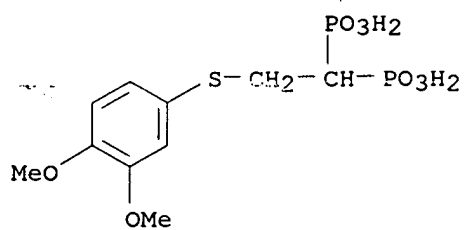
RN 221003-11-8 CAPLUS

CN Phosphonic acid, [2-[[4-(acetamino)phenyl]thio]ethylidene]bis- (9CI)  
(CA INDEX NAME)



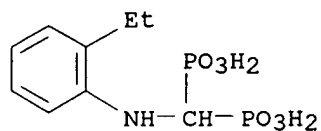
RN 221003-13-0 CAPLUS

CN Phosphonic acid, [2-[(3,4-dimethoxyphenyl)thio]ethylidene]bis- (9CI) (CA INDEX NAME)



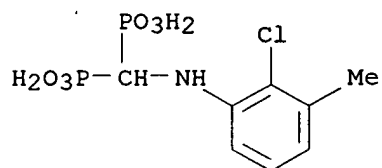
RN 221003-14-1 CAPLUS

CN Phosphonic acid, [[(2-ethylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 221003-16-3 CAPLUS

CN Phosphonic acid, [[(2-chloro-3-methylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1997:389221 CAPLUS  
 DOCUMENT NUMBER: 127:5356  
 TITLE: Preparation of peptides as inhibitors of  
 proliferation  
 of smooth muscle cells  
 INVENTOR(S): Nakahara, Yo; Hara, Saburo; Kamikubo, Yuichi;  
 Takemoto, Sumiyo; Miyamoto, Seiji  
 PATENT ASSIGNEE(S): Juridical Foundation the Chemo-Sero-Therapeutic  
 Research Institute, Japan; Nakahara, Yo; Hara,  
 Saburo;  
 Kamikubo, Yuichi; Takemoto, Sumiyo; Miyamoto, Seiji  
 SOURCE: PCT Int. Appl., 45 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715598	A1	19970501	WO 1996-JP3080	19961023
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,				
SE				
CA 2232240	AA	19970501	CA 1996-2232240	19961023
AU 9673357	A1	19970515	AU 1996-73357	19961023
AU 719366	B2	20000504		
EP 867450	A1	19980930	EP 1996-935411	19961023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, FI				
PRIORITY APPLN. INFO.:			JP 1995-300792	19951024
			WO 1996-JP3080	19961023

OTHER SOURCE(S): MARPAT 127:5356

AB Disclosed is a peptide contg. a peptide (A) consisting of an amino acid  
 sequence rich in basic amino acids and another peptide (B) consisting of  
 an amino acid sequence contg. at least two consecutive hydrophobic amino  
 acid residues wherein the peptide (B) is bonded directly or via an amino  
 acid sequence consisting of several amino acids to the C-terminus of the  
 peptide (A). This novel peptide has an excellent inhibitory effect on

the

proliferation of smooth muscle fibers and pharmaceutical preps.  
 contg. the peptide are efficacious in the prevention or treatment of  
 arteriosclerosis accompanying the proliferation of smooth muscle fibers,  
 restenosis after angioplasty, luminal stenosis after vascular  
 transplantation, and leiomyosarcoma. Thus, 20 peptides related to the  
 C-terminus region of tissue factor pathway inhibitor  
 (TFPI), e.g. H-KTKRKRKKQVRVKIAYEEIFVKNM-OH (I), were prepd. by the solid  
 phase method. I in vitro dose-dependently inhibited the proliferation of  
 smooth muscle cell of human aorta blood vessels.

IT 194554-71-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); USES (Uses)

(C-terminus peptide analogs; prepn. of tissue factor  
 pathway inhibitor peptide analogs as inhibitors of proliferation of

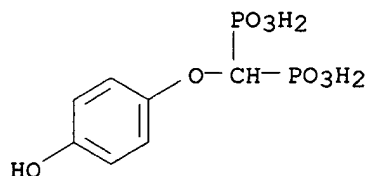
smooth muscle cells for disease therapy)  
RN 194554-71-7 CAPLUS  
CN Proteinase inhibitor, TFPI (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

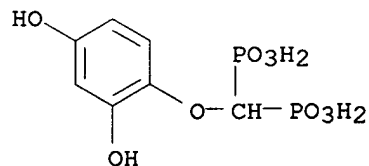
ACCESSION NUMBER: 1994:219245 CAPLUS  
 DOCUMENT NUMBER: 120:219245  
 TITLE: Polyanilines Doped with Phosphonic Acids: Their Preparation and Characterization  
 AUTHOR(S): Chan, H. S. O.; Ng, S. C.; Ho, P. K. H.  
 CORPORATE SOURCE: Department of Chemistry, National University of Singapore, Singapore, 0511, Singapore  
 SOURCE: Macromolecules (1994), 27(8), 2159-64  
 CODEN: MAMOBX; ISSN: 0024-9297  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Highly conducting polyaniline (I) with thermal stabilities superior to that of I doped with HCl have been prepd. by postsynthesis treatment of the I-base with 3 different phosphonic acids, RPA, where R = Bu, decyl, and benzyl (Bn). XPS results indicate the occurrence of free dopant mols. in the sample matrix, partial segregation of dopant species to the polymer surface, and participation of H3O+ as counter charges to some of the dopant anions in these samples. IR data suggest minimal perturbation of the I vibrational states when Cl- is replaced by RPO2(OH)-. Isothermal studies show the vastly superior thermal stabilities of the I-RPA over those of I-HCl. Thermogravimetric anal. has demonstrated a condensation reaction above 150.degree. among the POH and NH functions to give a crosslinked structure with loss of elec. cond. The stepwise doping process of I-base by different amts. of BnPA was followed closely by UV-visible spectroscopy.  
 IT **6881-57-8P**  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (dopant, prepn. of, for polyaniline)  
 RN 6881-57-8 CAPLUS  
 CN Phosphonic acid, (phenylmethyl)- (9CI) (CA INDEX NAME)

Ph-CH<sub>2</sub>-PO<sub>3</sub>H<sub>2</sub>

ACCESSION NUMBER: 1993:428231 CAPLUS  
 DOCUMENT NUMBER: 119:28231  
 TITLE: 4-Hydroxyphenoxymethylene bisphosphonic acid  
 derivatives: potent, non-hydrolyzable inhibitors of  
 myo-inositol monophosphatase  
 AUTHOR(S): Fletcher, Stephen R.; Baker, Raymond; Ladduwahetty,  
 Tamara; Sharpe, Andrew; Teall, Martin; Atack, John R.  
 CORPORATE SOURCE: Neurosci. Res. Cent., Merck, Sharp and Dohme Res.  
 Lab., Terlings Park/Harlow, UK  
 SOURCE: Bioorg. Med. Chem. Lett. (1993), 3(2), 141-6  
 CODEN: BMCLE8; ISSN: 0960-894X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 119:28231  
 AB From a series of 4-hydroxyphenoxymethylene bisphosphonic acid derivs.,  
 1-(4-hydroxyphenoxy)-1-(methyl)methylenebisphosphonic acid was  
 identified  
 as a structurally simple, competitive inhibitor of myo-inositol  
 monophosphatase (IC<sub>50</sub>, 0.33 .mu.M). Replacement of the 1-Me group by a  
 3-(3,4-dichlorobenzamido)benzyl substituent affords the most potent  
 inhibitor of the series (IC<sub>50</sub>, 0.08 .mu.M).  
 IT **104407-97-8P 147875-55-6P**  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. and inhibition by, of myo-inositol monophosphatase)  
 RN 104407-97-8 CAPLUS  
 CN Phosphonic acid, [(4-hydroxyphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



RN 147875-55-6 CAPLUS  
 CN Phosphonic acid, [(2,4-dihydroxyphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1996:705780 CAPLUS  
 DOCUMENT NUMBER: 125:320562  
 TITLE: Preparation of herbicidal bisphosphonic acids  
 INVENTOR(S): Fisher, Karl J.; Woolard, Frank X.; Leadbetter,  
 Michael R.; Gerdes, John M.  
 PATENT ASSIGNEE(S): Zeneca Limited, UK  
 SOURCE: PCT Int. Appl., 58 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9631124	A1	19961010	WO 1996-US4869	19960408
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN			
US 5728650	A	19980317	US 1995-418970	19950407
AU 9654475	A1	19961023	AU 1996-54475	19960408
EP 820230	A1	19980128	EP 1996-911660	19960408
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI			
BR 9604975	A	19980609	BR 1996-4975	19960408
JP 11503429	T2	19990326	JP 1996-530540	19960408
NO 9704619	A	19971006	NO 1997-4619	19971006
PRIORITY APPLN. INFO.:			US 1995-418970	19950407
			US 1993-133722	19931007
			WO 1996-US4869	19960408

OTHER SOURCE(S): MARPAT 125:320562

AB The bisphosphonic acids R6R7NCR4R5(CR2R3)nCR1(PO3H2)2 [n = 1-6; R1 = H, OH, alkoxy, halo, etc.; R2-5 = H = (un)substituted hydrocarbyl, etc.; R6,R7 = H, (un)substituted hydrocarbyl, (un)substituted pyridyl, (un)substituted amine, etc.; R6NR7 = piperazine, aziridine, morpholine, etc.] or their salts or hydrolyzable esters are prepd. as herbicides.

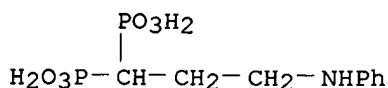
The herbicidal compns. exhibit efficacy when applied to plants post-emergence, but not pre-emergence.

IT 183446-62-0P 183446-77-7P 183446-85-7P  
 183447-31-6P 183447-32-7P 183447-35-0P  
 183447-36-1P

RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
 (prepn. as herbicide)

RN 183446-62-0 CAPLUS

CN Phosphonic acid, [3-(phenylamino)propylidene]bis- (9CI) (CA INDEX NAME)





=> s l15/prep

9 L15  
2614414 PREP/RL  
L17 7 L15/PREP  
(L15 (L) PREP/RL)

=> s l14/prep

49 L14  
2614414 PREP/RL  
L18 26 L14/PREP  
(L14 (L) PREP/RL)

=> d ibib abs hitstr 1-26

L18 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:162340 CAPLUS

DOCUMENT NUMBER: 130:209820

TITLE: Substituted 1,1-bisphosphonates for use as enzyme inhibitors and drugs

INVENTOR(S): Brands, Michael; Lohrmann, Emanuel; Schmidt, Delf; Kirsten, Rolf; Riebel, Hans-Joachim; Eckenberg, Peter;

Hansen, Jutta; Raddatz, Siegfried; Schulze, Thomas; Trappe, Joerg

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Ger. Offen., 68 pp.

CODEN: GWXXBX

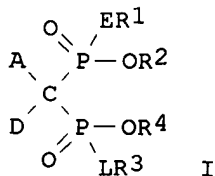
DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19738005	A1	19990304	DE 1997-19738005	19970830
OTHER SOURCE(S): MARPAT 130:209820				
GI				

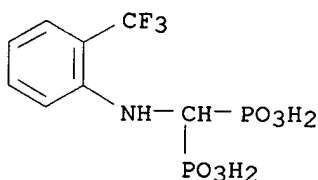


AB Substituted 1,1-bisphosphonates [I; R1-R4 = H, C1-5 alkyl; A =

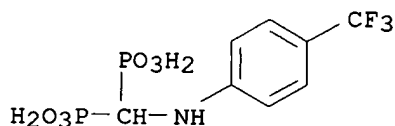
(CO)a(CH<sub>2</sub>)bNR<sub>5</sub>R<sub>6</sub>, CH<sub>2</sub>SCR<sub>7</sub>, C(S)NHR<sub>8</sub>; D = H; or AD = :O, :CHR<sub>11</sub>, :NR<sub>12</sub>; R<sub>5</sub> = H, C<sub>1</sub>-6 alkyl; R<sub>6</sub> = H, C<sub>1</sub>-5 alkyl, cycloalkyl, (substituted) aryl, heteroaryl, etc.; R<sub>7</sub>, R<sub>8</sub> = C<sub>3</sub>-7 cycloalkyl, (substituted) aryl, heteroaryl, etc.; R<sub>11</sub>, R<sub>12</sub> = 2-fluorenyl, 4-benzyloxyphenyl, 9-phenanthryl, 2-thiazolyl, etc.; E, L = O, S; a, b, c = 0, 1] and their salts, enantiomers, and diastereomers are prepd. which (a) inhibit protein phosphatase 1 and are useful for treatment of cardiovascular disorders, and/or (b) inhibit HIV integrase and are useful for prevention and treatment of retroviral infections (no data). I are prepd. (a) by addn. reaction of tetra-Et vinylidene-1,1-bisphosphonate with appropriate thiols or amines, (b) by condensation of tetra-Et methylenebisphosphonate with appropriate bromomethyl compds., isocyanates, or aldehydes, or (c) by reaction of phosphite esters with appropriate amines and orthoformates or with R<sub>12</sub>N:CCl<sub>2</sub>. Thus, cyclohexanethiol reacted with di-Et [1-(diethoxyphosphino)vinyl]phosphonate to form di-Et [2-(cyclohexylthio)-1-(diethoxyphosphino)ethyl]phosphonate, which was converted to the free acid with BrSiMe<sub>3</sub>.

IT 221002-55-7P 221002-58-0P 221002-90-0P  
 221002-98-8P 221003-03-8P 221003-05-0P  
 221003-09-4P 221003-10-7P 221003-14-1P  
 221003-16-3P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP** (Preparation); USES (Uses)  
 (substituted bisphosphonates for use as enzyme inhibitors and drugs)

RN 221002-55-7 CAPLUS  
 CN Phosphonic acid, [[[2-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI)  
 (CA INDEX NAME)

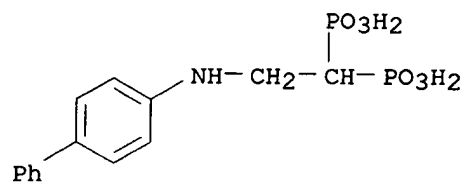


RN 221002-58-0 CAPLUS  
 CN Phosphonic acid, [[[4-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI)  
 (CA INDEX NAME)



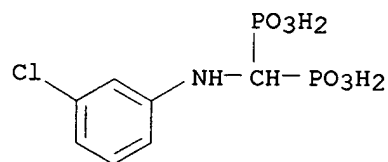
RN 221002-90-0 CAPLUS  
 CN Phosphonic acid, [2-([1,1'-biphenyl]-4-ylamino)ethylidene]bis- (9CI) (CA

INDEX NAME)



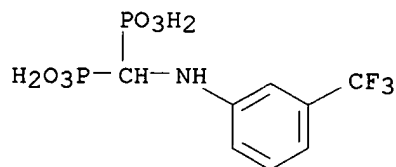
RN 221002-98-8 CAPLUS

CN Phosphonic acid, [[(3-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



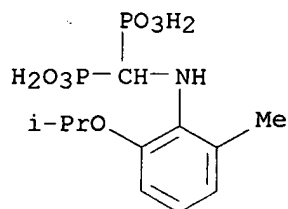
RN 221003-03-8 CAPLUS

CN Phosphonic acid, [[[3-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 221003-05-0 CAPLUS

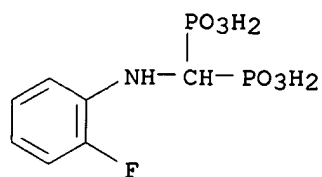
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RN 221003-09-4 CAPLUS

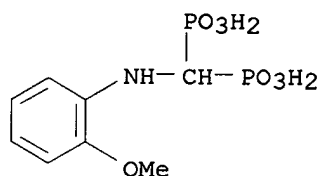
CN Phosphonic acid, [[(2-fluorophenyl)amino]methylene]bis- (9CI) (CA INDEX

NAME)



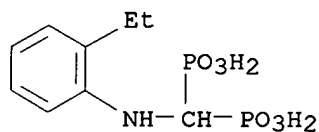
RN 221003-10-7 CAPLUS

CN Phosphonic acid, [[(2-methoxyphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



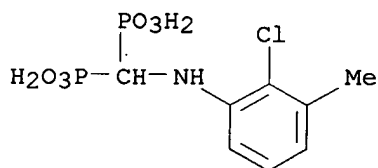
RN 221003-14-1 CAPLUS

CN Phosphonic acid, [[(2-ethylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 221003-16-3 CAPLUS

CN Phosphonic acid, [[(2-chloro-3-methylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:186482 CAPLUS

DOCUMENT NUMBER: 128:240717

TITLE: Preparation of herbicidal azabisphosphonic acids

INVENTOR(S): Fisher, Karl J.; Woolard, Frank X.; Leadbetter, Michael R.; Gerdes, John M.

PATENT ASSIGNEE(S): Zeneca Ltd., UK  
 SOURCE: U.S., 43 pp. Cont.-in-part of U.S. Ser. No. 133,722,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5728650	A	19980317	US 1995-418970	19950407
ZA 9407814	A	19950814	ZA 1994-7814	19941006
CA 2173607	AA	19950420	CA 1994-2173607	19941007
CN 1134657	A	19961030	CN 1994-194096	19941007
HU 74893	A2	19970228	HU 1996-839	19941007
WO 9631124	A1	19961010	WO 1996-US4869	19960408
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2217655	AA	19961010	CA 1996-2217655	19960408
AU 9654475	A1	19961023	AU 1996-54475	19960408
EP 820230	A1	19980128	EP 1996-911660	19960408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1181690	A	19980513	CN 1996-193132	19960408
BR 9604975	A	19980609	BR 1996-4975	19960408
JP 11503429	T2	19990326	JP 1996-530540	19960408
NO 9704619	A	19971006	NO 1997-4619	19971006
PRIORITY APPLN. INFO.:			US 1993-133722	19931007
			US 1995-418970	19950407
			WO 1996-US4869	19960408

OTHER SOURCE(S): MARPAT 128:240717

AB The azabisphosphonic acids R6R7NCR4R5(CR2R3)nCR1(PO3H2)2 [n = 0, 1-6; R1 =

H, OH, alkyl, alkoxy, halo, etc.; R2-5 H, (un)substituted hydrocarbonyl, etc.; R6, R7 = R2, (un)substituted pyridyl or (un)substituted amino; R6R7N, R4R6CN or R2R6CN = (un)substituted N-contg. heterocyclyl; R2R4C

and

R4R5C = (un)substituted carbocyclyl] and their salts or hydrolyzable esters are prepd. as postemergence herbicides.

IT 166747-10-0P 172957-71-0P 183446-62-0P

183446-77-7P 183446-85-7P 183447-31-6P

183447-32-7P 183447-35-0P 183447-36-1P

204984-04-3P 204984-10-1P 204984-15-6P

204984-16-7P 204984-18-9P 204984-21-4P

204984-22-5P 204984-23-6P 204984-24-7P

204984-25-8P 204984-26-9P 204984-27-0P

204984-41-8P 204984-42-9P 204984-43-0P

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204984-91-8P 204985-19-3P 204985-68-2P

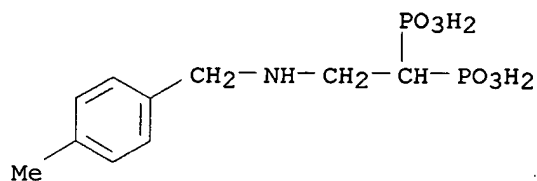
204985-78-4P 204986-39-0P 204986-41-4P

RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological

study); **PREP (Preparation)**; **USES (Uses)**  
(prepn. as herbicide)

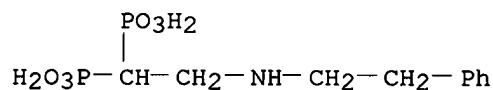
RN 166747-10-0 CAPLUS

CN Phosphonic acid, [2-[[[4-methylphenyl)methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME).



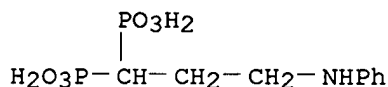
RN 172957-71-0 CAPLUS

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INDEX NAME)



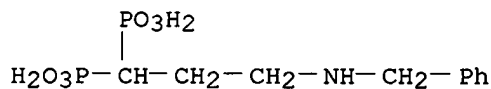
RN 183446-62-0 CAPLUS

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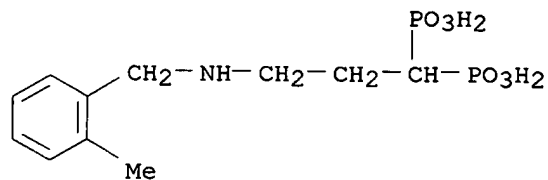
RN 183446-77-7 CAPLUS

CN Phosphonic acid, [3-[(phenylmethyl)amino]propylidene]bis- (9CI) (CA  
INDEX NAME)



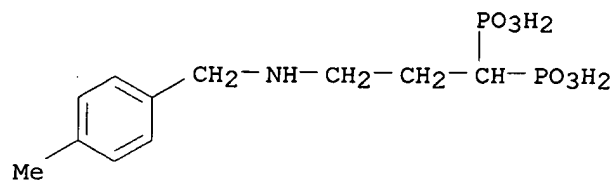
RN 183446-85-7 CAPLUS

CN Phosphonic acid, [3-[[[2-methylphenyl)methyl]amino]propylidene]bis- (9CI)  
(CA INDEX NAME)



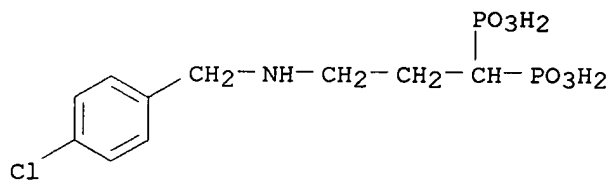
RN 183447-31-6 CAPLUS

CN Phosphonic acid, [3-[[ (4-methylphenyl)methyl]amino]propylidene]bis- (9CI)  
(CA INDEX NAME)



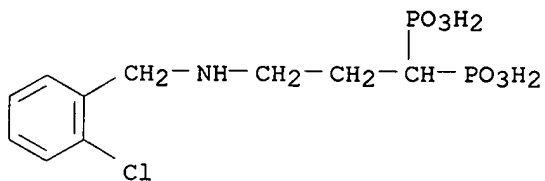
RN 183447-32-7 CAPLUS

CN Phosphonic acid, [3-[[ (4-chlorophenyl)methyl]amino]propylidene]bis- (9CI)  
(CA INDEX NAME)



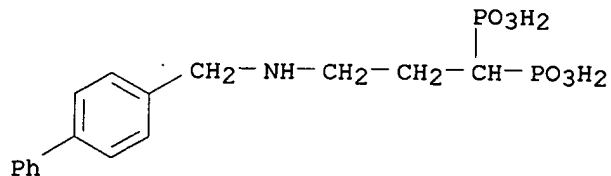
RN 183447-35-0 CAPLUS

CN Phosphonic acid, [3-[[ (2-chlorophenyl)methyl]amino]propylidene]bis- (9CI)  
(CA INDEX NAME)

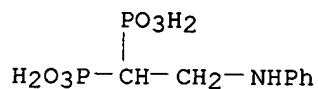


RN 183447-36-1 CAPLUS

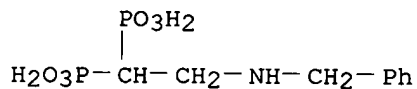
CN Phosphonic acid, [3-[[ ([1,1'-biphenyl]-4-ylmethyl)amino]propylidene]bis-  
(9CI) (CA INDEX NAME)



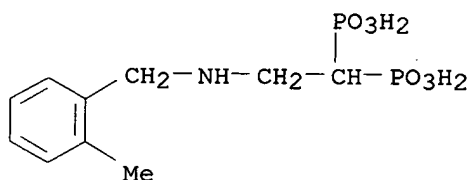
RN 204984-04-3 CAPLUS  
 CN Phosphonic acid, [2-(phenylamino)ethylidene]bis- (9CI) (CA INDEX NAME)



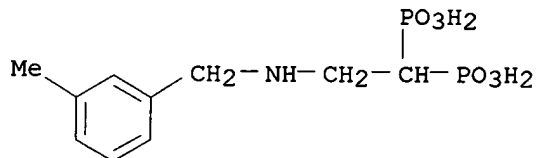
RN 204984-10-1 CAPLUS  
 CN Phosphonic acid, [2-[(phenylmethyl)amino]ethylidene]bis- (9CI) (CA INDEX NAME)



RN 204984-15-6 CAPLUS  
 CN Phosphonic acid, [2-[(2-methylphenyl)methyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)



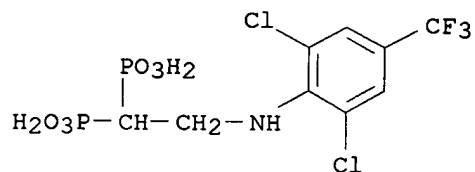
RN 204984-16-7 CAPLUS  
 CN Phosphonic acid, [2-[(3-methylphenyl)methyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)



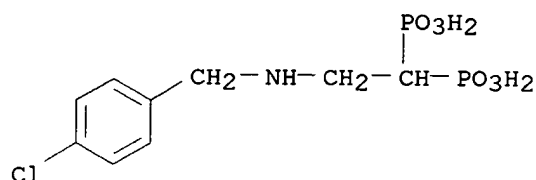
RN 204984-18-9 CAPLUS



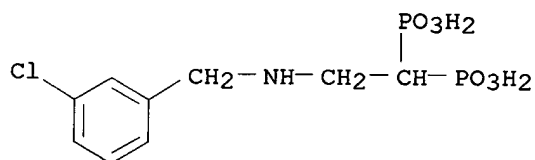
CN Phosphonic acid,  
[2-[[2,6-dichloro-4-(trifluoromethyl)phenyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)



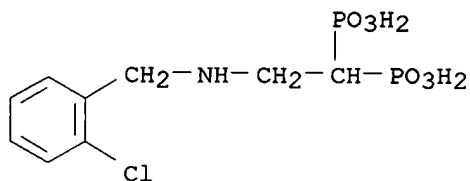
RN 204984-21-4 CAPLUS  
CN Phosphonic acid, [2-[[4-chlorophenyl)methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)



RN 204984-22-5 CAPLUS  
CN Phosphonic acid, [2-[[3-chlorophenyl)methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)

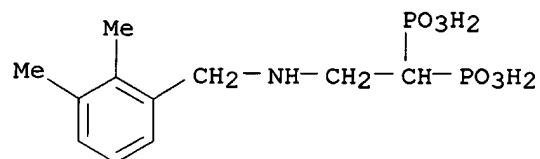


RN 204984-23-6 CAPLUS  
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(CA INDEX NAME)

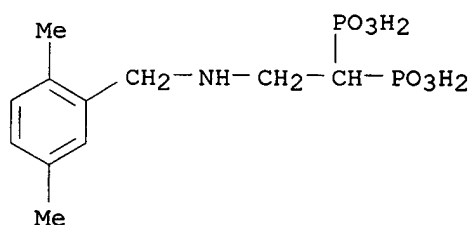


RN 204984-24-7 CAPLUS  
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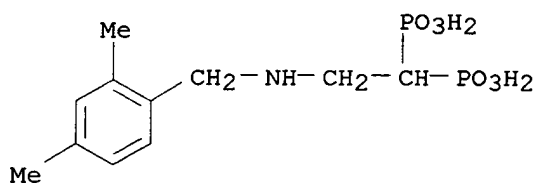
(9CI) (CA INDEX NAME)



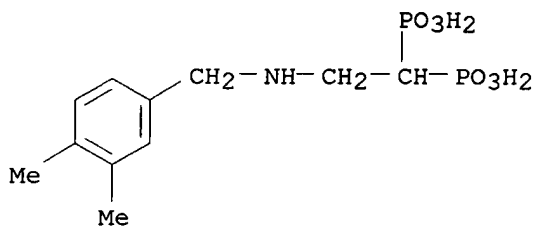
RN 204984-25-8 CAPLUS

CN Phosphonic acid, [2-[[ (2,5-dimethylphenyl)methyl]amino]ethylidene]bis-  
(9CI) (CA INDEX NAME)

RN 204984-26-9 CAPLUS

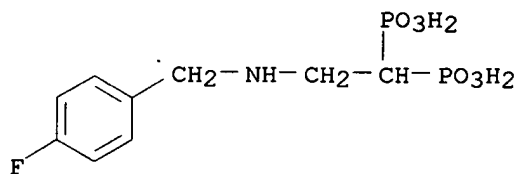
CN Phosphonic acid, [2-[[ (2,4-dimethylphenyl)methyl]amino]ethylidene]bis-  
(9CI) (CA INDEX NAME)

RN 204984-27-0 CAPLUS

CN Phosphonic acid, [2-[[ (3,4-dimethylphenyl)methyl]amino]ethylidene]bis-  
(9CI) (CA INDEX NAME)

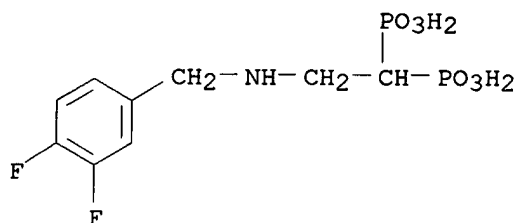
RN 204984-41-8 CAPLUS

CN Phosphonic acid, [2-[[ (4-fluorophenyl)methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)



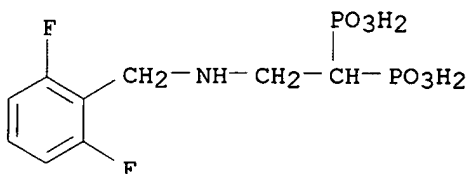
RN 204984-42-9 CAPLUS

CN Phosphonic acid, [2-[[ (3,4-difluorophenyl)methyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)



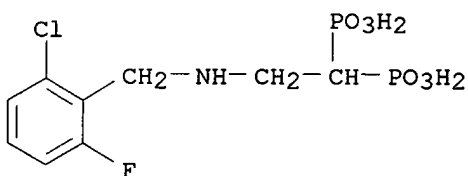
RN 204984-43-0 CAPLUS

CN Phosphonic acid, [2-[[ (2,6-difluorophenyl)methyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)



RN 204984-44-1 CAPLUS

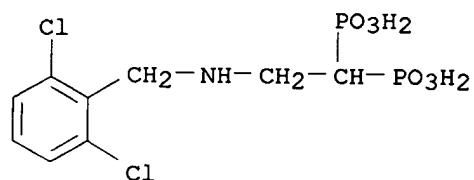
CN Phosphonic acid, [2-[[ (2-chloro-6-fluorophenyl)methyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)



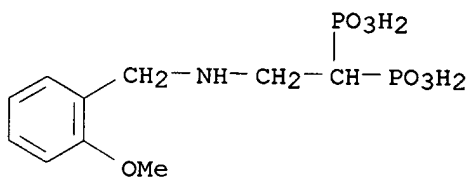
RN 204984-45-2 CAPLUS

CN Phosphonic acid, [2-[[ (2,6-dichlorophenyl)methyl]amino]ethylidene]bis-

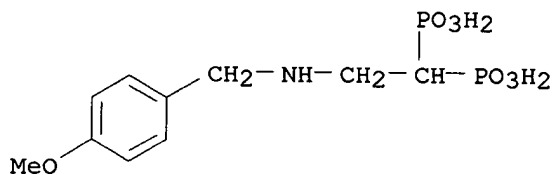
(9CI) (CA INDEX NAME)



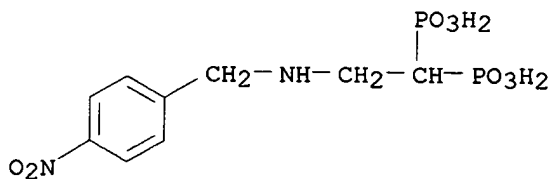
RN 204984-59-8 CAPLUS

CN Phosphonic acid, [2-[[2-methoxyphenyl]methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)

RN 204984-91-8 CAPLUS

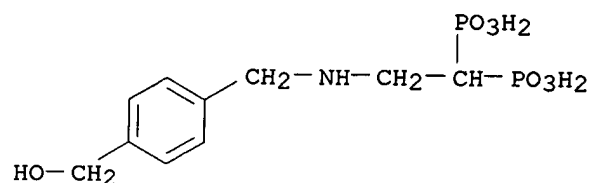
CN Phosphonic acid, [2-[[4-methoxyphenyl]methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)

RN 204985-19-3 CAPLUS

CN Phosphonic acid, [2-[[4-nitrophenyl]methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)

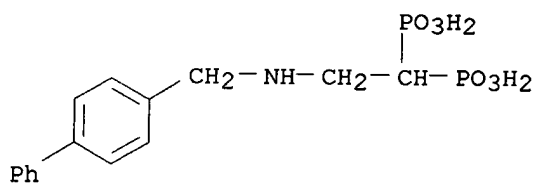
RN 204985-68-2 CAPLUS

CN Phosphonic acid,  
[2-[[[4-(hydroxymethyl)phenyl]methyl]amino]ethylidene]bis-  
(9CI) (CA INDEX NAME)



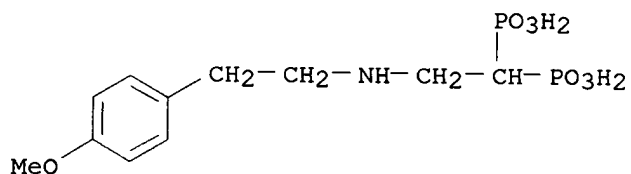
RN 204985-78-4 CAPLUS

CN Phosphonic acid, [2-[[[1,1'-biphenyl]-4-ylmethyl)amino]ethylidene]bis-  
(9CI) (CA INDEX NAME)



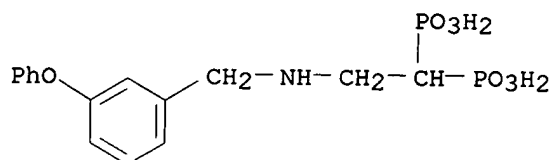
RN 204986-39-0 CAPLUS

CN Phosphonic acid, [2-[[2-(4-methoxyphenyl)ethyl]amino]ethylidene]bis-  
(9CI)  
(CA INDEX NAME)



RN 204986-41-4 CAPLUS

CN Phosphonic acid, [2-[[[3-phenoxyphenyl)methyl]amino]ethylidene]bis- (9CI)  
(CA INDEX NAME)

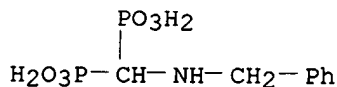


L18 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1998:38896 CAPLUS  
DOCUMENT NUMBER: 128:61631

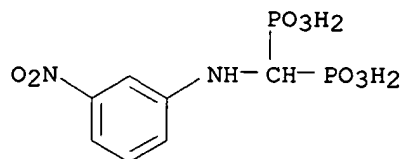
TITLE: Preparation of novel derivatives of  
(aminomethylene)bis(phosphonic acid) as herbicides  
INVENTOR(S): Soloducho, Jadwiga; Gancarz, Roman; Wieczorek, Piotr;  
Korf, Joanna; Hafner, Joanna; Lejczak, Barbara;  
Kafarski, Pawel  
PATENT ASSIGNEE(S): Politechnika Wroclawska, Pol.; Wyzsza Szkola  
Pedagogiczna  
SOURCE: Pol., 3 pp.  
CODEN: POXXA7  
DOCUMENT TYPE: Patent  
LANGUAGE: Polish  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 172268	B1	19970829	PL 1993-298436	19930408

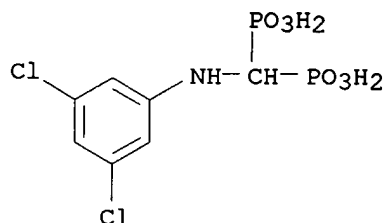
OTHER SOURCE(S): CASREACT 128:61631; MARPAT 128:61631  
AB Title compds. RR1NCH(PO3H2)2 (R = H; Ph; C6H4X, C6H3X2, X = Cl, Br; C6H4NO2; benzyl; C3-6 cycloalkyl; C1-6 alkyl; R1 = H; RR1 = oxydiethylene), useful as herbicides, are prepd. by heating to reflux an aliph., alicyclic, or arom. amine with an alkyl orthoformate and a dialkyl phosphite, preferably di-Et, followed by hydrolysis of the crude product with HCl and isolation of the product by crystn. or ion-exchange chromatog. In an example, 0.05 mol m-nitroaniline is heated to reflux with an equimolar amt. of (EtO)3CH and 0.1 mol di-Et phosphite at 373 K for 12 h, whereupon the alc. formed is distd. off and the residue is crystd. and hydrolyzed in 20 cm3 6N HCl at 368 K to afford 80% m-O2NC6H4NHCH(PO3H2)2. This compd. inhibited the growth of Lepidium sativum up to 90% when applied in 5.0 mM concn. to the roots of the plants.  
IT **32545-71-4P 194999-99-0P 195000-01-2P**  
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
(prepn. of (aminomethylene)bis(phosphonic acid) derivs. as herbicides)  
RN 32545-71-4 CAPLUS  
CN Phosphonic acid, [[(phenylmethyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 194999-99-0 CAPLUS  
CN Phosphonic acid, [[[3-nitrophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 195000-01-2 CAPLUS  
 CN Phosphonic acid, [[(3,5-dichlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1997:596830 CAPLUS  
 DOCUMENT NUMBER: 127:216305  
 TITLE: Herbicidal derivatives of aminomethylenebisphosphonic acid. Part III. Structure-activity relationship  
 AUTHOR(S): Kafarski, P.; Lejczak, B.; Forlani, G.; Gancarz, R.; Torreilles, C.; Grembecka, J.; Ryzek, A.; Wieczorek, P.  
 CORPORATE SOURCE: Institute of Organic Chemistry, Biochemistry, and Biotechnology, Technical University of Wroclaw, Wroclaw, 50-370, Pol.  
 SOURCE: J. Plant Growth Regul. (1997), 16(3), 153-158  
 CODEN: JPGRDI; ISSN: 0721-7595  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Derivs. of aminomethylenebisphosphonic acids constitute a class of promising herbicides. More than 40 N-substituted aminomethylenephosphonic

acids were synthesized and evaluated for their herbicidal activity on common cress (*Lepidium sativum* L.) and cucumber (*Cucumis sativus* L.). Some of the tested compds. were found to exhibit strong herbicidal properties being equal in activity with the popular herbicide glyphosate as well as parent N-pyridylaminomethylenephosphonic acids. N-Substituted iminodi(methylenephosphonic) acids, which may be considered as close analog of glyphosate, were inactive toward test plants.

IT 73269-57-5P 194999-99-0P 195000-00-1P  
 195000-01-2P 195000-02-3P 195000-03-4P  
 195000-04-5P 195000-05-6P 195001-38-8P

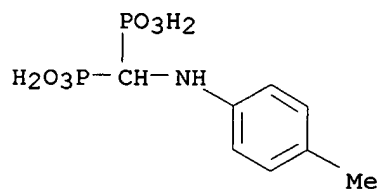
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**

(prepn. and herbicidal activity of aminomethylenebisphosphonic acid and

their structure-activity relationship)

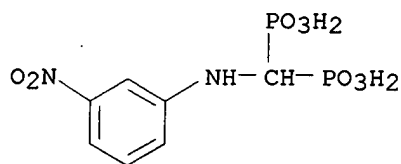
RN 73269-57-5 CAPLUS

CN Phosphonic acid, [[(4-methylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



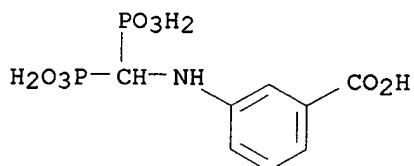
RN 194999-99-0 CAPLUS

CN Phosphonic acid, [[(3-nitrophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



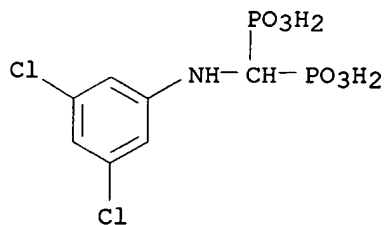
RN 195000-00-1 CAPLUS

CN Benzoic acid, 3-[(diphosphonomethyl)amino]- (9CI) (CA INDEX NAME)



RN 195000-01-2 CAPLUS

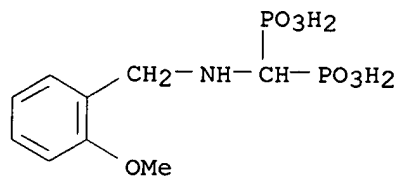
CN Phosphonic acid, [[(3,5-dichlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 195000-02-3 CAPLUS

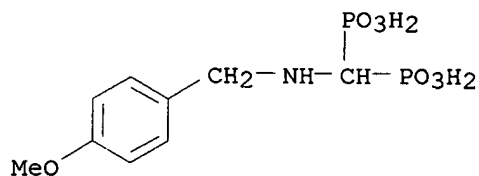


CN Phosphonic acid, [[[(2-methoxyphenyl)methyl]amino]methylene]bis- (9CI)  
(CA INDEX NAME)



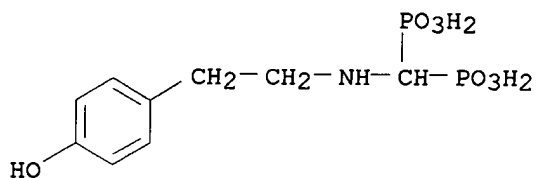
RN 195000-03-4 CAPLUS

CN Phosphonic acid, [[[(4-methoxyphenyl)methyl]amino]methylene]bis- (9CI)  
(CA INDEX NAME)



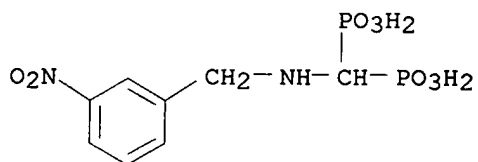
RN 195000-04-5 CAPLUS

CN Phosphonic acid, [[[(2-(4-hydroxyphenyl)ethyl]amino]methylene]bis- (9CI)  
(CA INDEX NAME)



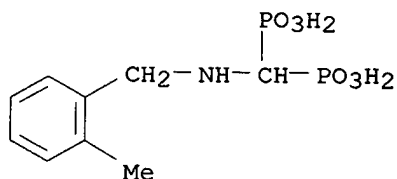
RN 195000-05-6 CAPLUS

CN Phosphonic acid, [[[(3-nitrophenyl)methyl]amino]methylene]bis- (9CI) (CA  
INDEX NAME)



RN 195001-38-8 CAPLUS

CN Phosphonic acid, [[[(2-methylphenyl)methyl]amino]methylene]bis- (9CI)  
(CA INDEX NAME)



L18 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:750334 CAPLUS

DOCUMENT NUMBER: 126:100638

TITLE: Mode of action of herbicidal derivatives of aminomethylenebisphosphonic acid. I. Physiologic activity and inhibition of anthocyanin biosynthesis  
 AUTHOR(S): Lejczak, B.; Boduszek, B.; Kafarski, P.; Forlani, G.; Wojtasek, H.; Wieczorek, P.

CORPORATE SOURCE: Institute Organic Chemistry, Biochemistry, & Biotechnology, Technical Univ. Wroclaw, Wroclaw, Pol.  
 SOURCE: J. Plant Growth Regul. (1996), 15(3), 109-113  
 CODEN: JPGRDI; ISSN: 0721-7595

PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N-Pyridylaminomethylenebisphosphonic acids constitute a class of promising

herbicides. Since their mode of action at the cellular level is still poorly understood, the authors studied the influence of N-pyridylaminomethylenebisphosphonic acids on plant growth, at the whole plant and undifferentiated tissue levels, using seedlings and cell suspension cultures of mono- and dicotyledonous species. These compds. exhibited strong herbicidal properties, being equipotent with glyphosate. Since they also depressed buck weed anthocyanin biosynthesis, the shikimate pathway could represent a site of action of N-pyridylaminomethylenebisphosphonic acids. Prepn. of the compds. is

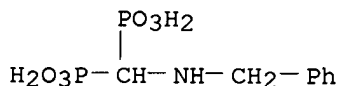
given.

IT 32545-71-4P

RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
 (prepn. and mechanism of herbicidal activity of)

RN 32545-71-4 CAPLUS

CN Phosphonic acid, [(phenylmethyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:705780 CAPLUS

DOCUMENT NUMBER: 125:320562

TITLE: Preparation of herbicidal bisphosphonic acids  
 INVENTOR(S): Fisher, Karl J.; Woolard, Frank X.; Leadbetter, Michael R.; Gerdes, John M.  
 PATENT ASSIGNEE(S): Zeneca Limited, UK  
 SOURCE: PCT Int. Appl., 58 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9631124	A1	19961010	WO 1996-US4869	19960408
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5728650	A	19980317	US 1995-418970	19950407
AU 9654475	A1	19961023	AU 1996-54475	19960408
EP 820230	A1	19980128	EP 1996-911660	19960408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9604975	A	19980609	BR 1996-4975	19960408
JP 11503429	T2	19990326	JP 1996-530540	19960408
NO 9704619	A	19971006	NO 1997-4619	19971006
PRIORITY APPLN. INFO.:				
			US 1995-418970	19950407
			US 1993-133722	19931007
			WO 1996-US4869	19960408

OTHER SOURCE(S): MARPAT 125:320562

AB The bisphosphonic acids R<sub>6</sub>R<sub>7</sub>NCR<sub>4</sub>R<sub>5</sub>(CR<sub>2</sub>R<sub>3</sub>)nCR<sub>1</sub>(PO<sub>3</sub>H<sub>2</sub>)<sub>2</sub> [n = 1-6; R<sub>1</sub> = H, OH, alkoxy, halo, etc.; R<sub>2</sub>-5 = H = (un)substituted hydrocarbyl, etc.; R<sub>6</sub>, R<sub>7</sub> = H, (un)substituted hydrocarbyl, (un)substituted pyridyl, (un)substituted amine, etc.; R<sub>6</sub>NR<sub>7</sub> = piperazine, aziridine, morpholine, etc.] or their salts or hydrolyzable esters are prep. as herbicides.

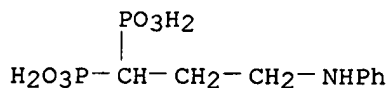
The herbicidal compns. exhibit efficacy when applied to plants post-emergence, but not pre-emergence.

IT 183446-62-0P 183446-77-7P 183446-85-7P  
 183447-31-6P 183447-32-7P 183447-35-0P  
 183447-36-1P

RL: AGR (Agricultural use); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)  
 (prepn. as herbicide)

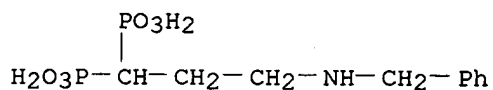
RN 183446-62-0 CAPLUS

CN Phosphonic acid, [3-(phenylamino)propylidene]bis- (9CI) (CA INDEX NAME)



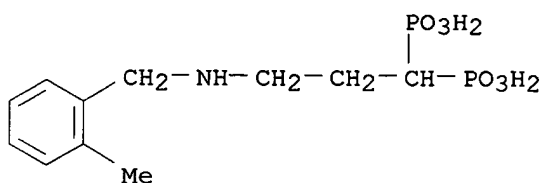
RN 183446-77-7 CAPLUS

CN Phosphonic acid, [3-[(phenylmethyl)amino]propylidene]bis- (9CI) (CA INDEX NAME)



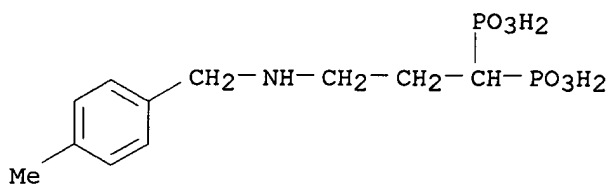
RN 183446-85-7 CAPLUS

CN Phosphonic acid, [3-[(2-methylphenyl)methyl]amino]propylidene]bis- (9CI) (CA INDEX NAME)



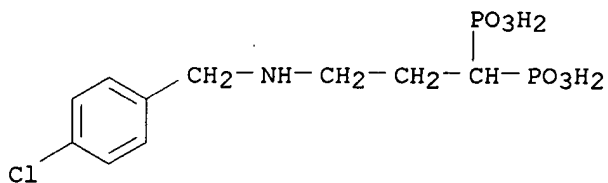
RN 183447-31-6 CAPLUS

CN Phosphonic acid, [3-[(4-methylphenyl)methyl]amino]propylidene]bis- (9CI) (CA INDEX NAME)



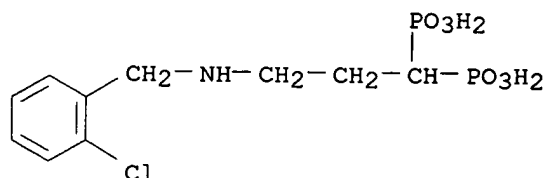
RN 183447-32-7 CAPLUS

CN Phosphonic acid, [3-[(4-chlorophenyl)methyl]amino]propylidene]bis- (9CI) (CA INDEX NAME)

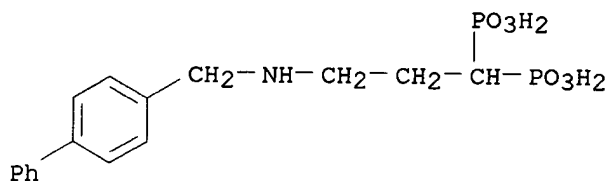


RN 183447-35-0 CAPLUS

CN Phosphonic acid, [3-[(2-chlorophenyl)methyl]amino]propylidene]bis- (9CI) (CA INDEX NAME)



RN 183447-36-1 CAPLUS  
 CN Phosphonic acid, [3-[[[1,1'-biphenyl]-4-ylmethyl)amino]propylidene]bis-  
 (9CI) (CA INDEX NAME)



L18 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1995:750617 CAPLUS  
 DOCUMENT NUMBER: 123:144276  
 TITLE: Herbicidal aza bisphosphonic acid compositions  
 INVENTOR(S): Fisher, Karl Joseph; Woolard, Frank Xavier; Gerdes, John Montgomery  
 PATENT ASSIGNEE(S): Zeneca Ltd., UK  
 SOURCE: PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9510188	A2	19950420	WO 1994-GB2183	19941007
WO 9510188	A3	19950504		
W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN			
RW:	KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
ZA 9407814	A	19950814	ZA 1994-7814	19941006
CA 2173607	AA	19950420	CA 1994-2173607	19941007
AU 9477901	A1	19950504	AU 1994-77901	19941007
AU 690581	B2	19980430		
EP 722268	A1	19960724	EP 1994-928482	19941007
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			

SE

CN 1134657	A	19961030	CN 1994-194096	19941007
HU 74893	A2	19970228	HU 1996-839	19941007
BR 9407762	A	19970304	BR 1994-7762	19941007
JP 09506075	T2	19970617	JP 1994-511442	19941007
NO 9601389	A	19960603	NO 1996-1389	19960403
FI 9601520	A	19960527	FI 1996-1520	19960404
PRIORITY APPLN. INFO.:			US 1993-133722	19931007
			WO 1994-GB2183	19941007

OTHER SOURCE(S): MARPAT 123:144276

AB The title compds. R4R5NCR2R3CR1(PO3H2)2 wherein R1 is hydrogen, hydroxy, C1-C4 alkoxy, halogen, C1-C4 alkyl, C1-C4 haloalkyl, hydroxy-C1-C4-alkyl, hydroxy-C1-C4-alkoxy or N(R6)(R7) wherein R6 and R7 are each

independently

H or C1-C3 alkyl; R2 and R3 are each independently H, hydrocarbyl, substituted hydrocarbyl, hydrocarbyloxy, substituted hydrocarbyloxy, hydrocarbyl-S(O)m, or substituted hydrocarbyl-S(O)m; or R2 and R3

together

from a 3-6 membered carbocyclic ring, optionally substituted with

halogen,

hydroxy, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 alkylthio or N(R8)(R9) wherein R8 and R9 are each independently H or C1-C12 alkyl; and R4 and R5 are

each

independently H, hydrocarbyl, substituted hydrocarbyl, hydrocarbyloxy, substituted hydrocarbyloxy, hydrocarbylthio, substituted pyridyl, or are N(R10)(R11) wherein R10 and R11 are independently H, hydrocarbyl or substituted hydrocarbyl; or R4 and R5 together with the N to which they are bound form an aziridine, piperazine, morpholine, thiomorpholine, thiomorpholine sulfinyl, thiomorpholine sulfonyl, hexamethyleneimine, piperidine, tetrahydropyridine, pyrazole, imidazole, pyrrole, triazole, tetrahydropyrimidine, dihydroimidazole, pyrroline, azetidine, perhydroindole, perhydroquinoline, perhydroisoquinoline or pyrrolidine ring, and of which may be optionally substituted with C1-C12 alkyl, halo, C6-C10 aryl etc. were prepd. A representative prepd. compd. is 2-[1-(1,2,4-triazole)]ethyl-1,1-bisphosphonic acid. In other aspects, this invention is directed to a method of controlling the growth of

plants

comprising applying to the area where control is desired an herbicidally effective amt. of the title compds.; as well as to certain novel compds. having a structure within the scope of the title compds.. above.

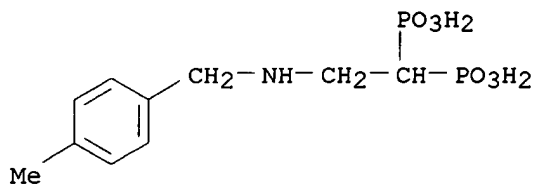
IT 166747-10-0P

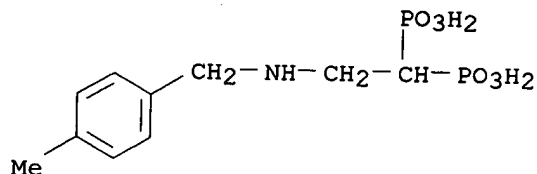
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation); USES (Uses)**

(prepn. of aminoethylidenediphosphonates as herbicides)

RN 166747-10-0 CAPLUS

CN Phosphonic acid, [2-[[[(4-methylphenyl)methyl]amino]ethylidene]bis- (9CI) (CA INDEX NAME)





L18 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1993:428231 CAPLUS

DOCUMENT NUMBER: 119:28231

TITLE: 4-Hydroxyphenoxymethylene bisphosphonic acid derivatives: potent, non-hydrolyzable inhibitors of myo-inositol monophosphatase

AUTHOR(S): Fletcher, Stephen R.; Baker, Raymond; Ladduwahetty, Tamara; Sharpe, Andrew; Teall, Martin; Atack, John R. Neurosci. Res. Cent., Merck, Sharp and Dohme Res. Lab., Terlings Park/Harlow, UK

CORPORATE SOURCE: Bioorg. Med. Chem. Lett. (1993), 3(2), 141-6  
CODEN: BMCLE8; ISSN: 0960-894X

SOURCE: Journal

DOCUMENT TYPE: English

LANGUAGE: English

OTHER SOURCE(S): CASREACT 119:28231

AB From a series of 4-hydroxyphenoxymethylene bisphosphonic acid derivs., 1-(4-hydroxyphenoxy)-1-(methyl)methylenebisphosphonic acid was identified

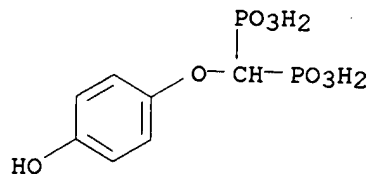
as a structurally simple, competitive inhibitor of myo-inositol monophosphatase (IC50, 0.33 .mu.M). Replacement of the 1-Me group by a 3-(3,4-dichlorobenzamido)benzyl substituent affords the most potent inhibitor of the series (IC50, 0.08 .mu.M).

IT 104407-97-8P 147875-55-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and inhibition by, of myo-inositol monophosphatase)

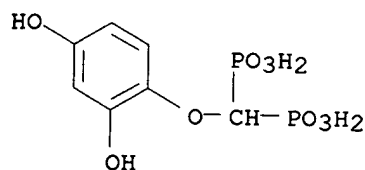
RN 104407-97-8 CAPLUS

CN Phosphonic acid, [(4-hydroxyphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



RN 147875-55-6 CAPLUS

CN Phosphonic acid, [(2,4-dihydroxyphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1991:247388 CAPLUS

DOCUMENT NUMBER: 114:247388

TITLE: Organic phosphorus compounds. 93. Preparation, properties and herbicidal activity of 2-substituted 5-phenoxy- and 5-pyridyloxy-phenylaminoalkyl-phosphonic- and -phosphinic acid as well as phosphine oxide derivatives

AUTHOR(S): Maier, Ludwig

CORPORATE SOURCE: Agric. Div., Ciba-Geigy A.-G., Basel, 4002, Switz.

SOURCE: Phosphorus, Sulfur Silicon Relat. Elem. (1991), 56(1-4), 5-15

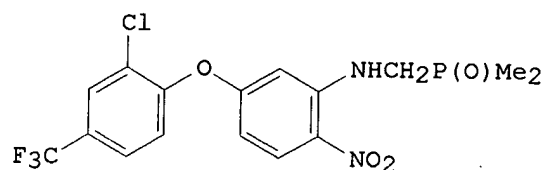
CODEN: PSSLEC; ISSN: 1042-6507

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 114:247388

GI



I

AB Interaction of 4-phenoxy and 4-pyridyloxy substituted 1,2-dinitrobenzenes and aminoalkylphosphonates, -phosphinates, and -phosphine oxides produces mainly 5-phenoxy and 5-pyridyloxy substituted 2-nitrophenylaminoalkylphosphonates, -phosphinates and -phosphine oxides, e.g., I, some of which show high herbicidal and plant growth regulating activity. The herbicidal activity increases from pyridyloxy-phenylaminoalkylphosphonates to phenoxy-phenylaminoalkyl-phosphonates, -phosphinates, and -phosphine oxides. Of all the compds. tested the phosphine oxide I was at all concns. the most active compd.

IT 89175-56-4P

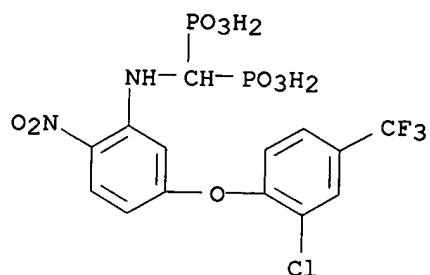
RL: SPN (Synthetic preparation); **PREP (Preparation)**

(prepn. and herbicidal and plant growth regulating activity of)

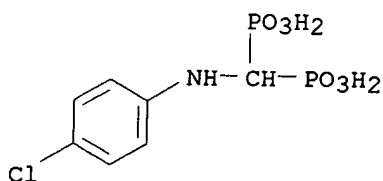
RN 89175-56-4 CAPLUS

CN Phosphonic acid, [[[5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrophenyl]amino]methylene]bis- (9CI) (CA INDEX NAME)

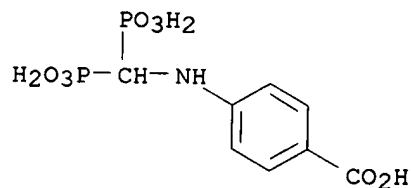




L18 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1990:552591 CAPLUS  
 DOCUMENT NUMBER: 113:152591  
 TITLE: New amino derivatives of methylenediphosphonic acid  
 as  
 complexes  
 AUTHOR(S): Gross, G.; Costisella, B.; Schwartz, K.; Kabachnik,  
 M.  
 CORPORATE SOURCE: I.; Bel'skii, F. I.; Polikarpov, Yu. M.  
 Inst. Elementoorg. Soedin. im. Nesmeyanova, Moscow,  
 USSR  
 SOURCE: Zh. Obshch. Khim. (1990), 60(4), 749-54  
 CODEN: ZOKHA4; ISSN: 0044-460X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB Three title compds.  $\text{RNHCH}[\text{P}(\text{O})(\text{OH})_2]_2$  ( $\text{R} = 2\text{-pyridyl}, 4\text{-HO}_2\text{CC}_6\text{H}_4,$   
 $4\text{-ClC}_6\text{H}_4$ ) were prepd. by known methods and the stability consts. of their  
 complexes with Mg, Ca, Mn, Co, Ni, Cu, Zn, and Cd dications were detd.  
 IT 59611-67-5DP, transition metal complexes 59611-69-7DP,  
 transition metal complexes  
 RL: **PREP (Preparation)**; PRP (Properties)  
 (formation and stability consts. of)  
 RN 59611-67-5 CAPLUS  
 CN Phosphonic acid, [[(4-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX  
 NAME)



RN 59611-69-7 CAPLUS  
 CN Benzoic acid, 4-[(diphosphonomethyl)amino]- (9CI) (CA INDEX NAME)

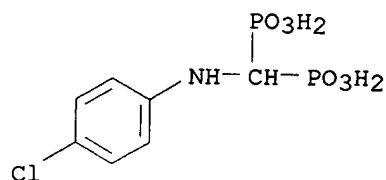


IT 59611-67-5P 59611-69-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and complexes of, with alkylene-earth and transition-metal  
dications, stability consts. of)

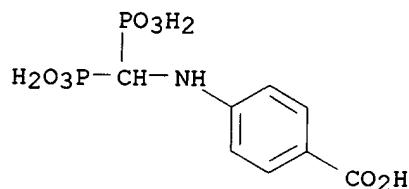
RN 59611-67-5 CAPLUS

CN Phosphonic acid, [[(4-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX  
NAME)



RN 59611-69-7 CAPLUS

CN Benzoic acid, 4-[(diphosphonomethyl)amino]- (9CI) (CA INDEX NAME)



L18 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1988:186840 CAPLUS

DOCUMENT NUMBER: 108:186840

TITLE: Iminobis(methylenediphosphonic acid)

AUTHOR(S): Alfer'ev, I. S.; Bobkov, S. Yu.; Kotlyarevskii, I. L.

CORPORATE SOURCE: Inst. Khim. Kinet. Goren., Novosibirsk, USSR

SOURCE: Izv. Akad. Nauk SSSR, Ser. Khim. (1987), (4), 865-8

CODEN: IASKA6; ISSN: 0002-3353

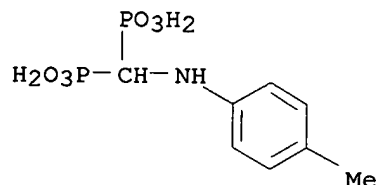
DOCUMENT TYPE: Journal

LANGUAGE: Russian

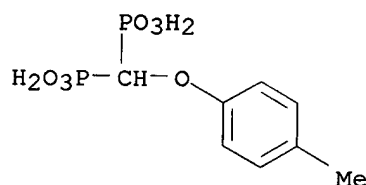
AB The effect of various additives (AlCl<sub>3</sub>, ZnCl<sub>2</sub>, p-MeC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, etc.) on the  
yield of HN[CH[P(O)(OH)<sub>2</sub>]<sub>2</sub>]<sub>2</sub> and H<sub>2</sub>NCH[P(O)(OH)<sub>2</sub>]<sub>2</sub> from the reaction of  
HCONH<sub>2</sub> with H<sub>3</sub>PO<sub>3</sub> and PX<sub>3</sub> (X = Cl, Br) was studied.

IT 73269-57-5P

RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)  
 RN 73269-57-5 CAPLUS  
 CN Phosphonic acid, [[(4-methylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)

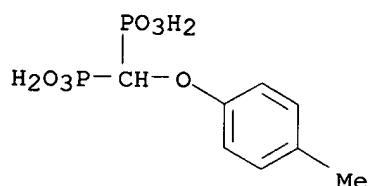


L18 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1988:94648 CAPLUS  
 DOCUMENT NUMBER: 108:94648  
 TITLE: Reaction of pyrophosphites with carboxylic acid esters  
 AUTHOR(S): Alfer'ev, I. S.; Bobkov, S. Yu.; Kotlyarevskii, I. L.  
 CORPORATE SOURCE: Inst. Khim. Kinet. Goren., Novosibirsk, USSR  
 SOURCE: Izv. Akad. Nauk SSSR, Ser. Khim. (1987), (3), 630-3  
 CODEN: IASKA6; ISSN: 0002-3353  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 OTHER SOURCE(S): CASREACT 108:94648  
 AB Reaction of [(RO)2P]2O (R2 = CH2CH2, R = Et, Me2CH) with R1O2CH (R1 = pentyl, Et, p-MeC6H4) in the presence of BF3 gave 0-63% (R1O)CH[P(O)(OH)2]2 and 69-5% (HO)CH[P(O)(OH)2]2.  
 IT **105810-40-0P**  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)  
 RN 105810-40-0 CAPLUS  
 CN Phosphonic acid, [(4-methylphenoxy)methylene]bis- (9CI) (CA INDEX NAME)

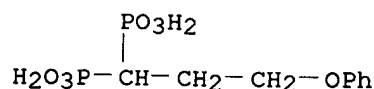


L18 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1988:94647 CAPLUS  
 DOCUMENT NUMBER: 108:94647  
 TITLE: 1-Alkoxy(aryloxy)alkylidene-1,1-diphosphonic acids  
 AUTHOR(S): Alfer'ev, I. S.; Bobkov, S. Yu.; Kotlyarevskii, I. L.  
 CORPORATE SOURCE: Inst. Khim. Kinet. Goren., Novosibirsk, USSR  
 SOURCE: Izv. Akad. Nauk SSSR, Ser. Khim. (1987), (3), 624-30

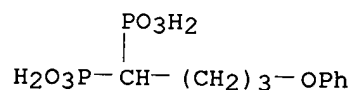
CODEN: IASKA6; ISSN: 0002-3353  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 OTHER SOURCE(S): CASREACT 108:94647  
 AB The title compds. were prepd. by treating alkyl carboxylates with a mixt. of H<sub>3</sub>PO<sub>3</sub> and PCl<sub>3</sub>, and with P<sub>4</sub>O<sub>6</sub> in the presence of BF<sub>3</sub>. Thus, treating HCO<sub>2</sub>R (R = Bu, pentyl, hexyl) with H<sub>3</sub>PO<sub>3</sub> and PCl<sub>3</sub> gave 10-15% ROCH[P(O)(OH)<sub>2</sub>]<sub>2</sub>.  
 IT **105810-40-0P**  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)  
 RN 105810-40-0 CAPLUS  
 CN Phosphonic acid, [(4-methylphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1987:459121 CAPLUS  
 DOCUMENT NUMBER: 107:59121  
 TITLE: gem-Diphosphonate and gem-phosphonate-phosphate compounds with specific high density lipoprotein inducing activity  
 AUTHOR(S): Nguyen Lan Mong; Niesor, Eric; Bentzen, Craig L.  
 CORPORATE SOURCE: Symphar S. A., Geneva, Switz.  
 SOURCE: J. Med. Chem. (1987), 30(8), 1426-33  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 107:59121  
 AB Title compds. [(RO)<sub>2</sub>P(O)]<sub>2</sub>CR<sub>1</sub>R<sub>2</sub> [R = Me, Et, Pr, Me<sub>2</sub>CH, Bu; R<sub>1</sub> = H, OH; R<sub>2</sub> = alkyl, (un)substituted aryl] and (RO)<sub>2</sub>P(O)CR<sub>1</sub>R<sub>2</sub>OP(O)(OR)<sub>2</sub> (I; same R-R<sub>2</sub>) were prepd. and examd. for activity in specifically inducing plasma high-d. lipoproteins (HDL) and HDL-cholesterol (HDL-C) in normal rats. Screening numerous compds. allowed detn. of structural variations leading to optimal plasma lipid-altering activity and antiatherosclerotic potential. I (R = Me; R<sub>1</sub> = H; R<sub>2</sub> = 4-ClC<sub>6</sub>H<sub>4</sub>) (SR-202, mifobate) was selected for further pharmacol. and subsequent clin. development.  
 IT **108816-80-4P 108816-81-5P**  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. and antiatherosclerotic activity of)  
 RN 108816-80-4 CAPLUS  
 CN Phosphonic acid, (3-phenoxypropylidene)bis- (9CI) (CA INDEX NAME)



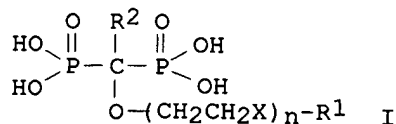
RN 108816-81-5 CAPLUS  
 CN Phosphonic acid, (4-phenoxybutylidene)bis- (9CI) (CA INDEX NAME)



L18 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1986:553318 CAPLUS  
 DOCUMENT NUMBER: 105:153318  
 TITLE: Methylenebis(phosphonic acid) derivatives  
 INVENTOR(S): Binderup, Ernst Torndal  
 PATENT ASSIGNEE(S): Leo Pharmaceutical Products Ltd., Den.  
 SOURCE: PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8600902	A1	19860213	WO 1985-DK71	19850725
W: AU, DK, FI, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
ZA 8505264	A	19860326	ZA 1985-5264	19850712
AU 8546736	A1	19860225	AU 1985-46736	19850725
AU 583848	B2	19890511		
EP 191044	A1	19860820	EP 1985-903807	19850725
EP 191044	B1	19900207		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 61503034	T2	19861225	JP 1985-503564	19850725
JP 06008303	B4	19940202		
AT 50262	E	19900215	AT 1985-903807	19850725
ES 545783	A1	19870901	ES 1985-545783	19850731
FI 8601357	A	19860327	FI 1986-1357	19860327
US 4732998	A	19880322	US 1986-852248	19860331
DK 8601473	A	19860401	DK 1986-1473	19860401
DK 167808	B1	19931220		
PRIORITY APPLN. INFO.:			GB 1984-19489	19840731
			EP 1985-903807	19850725
			WO 1985-DK71	19850725

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AB Phosphonates I [R<sup>1</sup> = (substituted) C<sub>1</sub>-10 (un)satd. alkyl, aralkyl; R<sup>2</sup> = H, C<sub>1</sub>-8 alkyl, aralkyl, halogen; X = O, S; n = 0 - 2; R<sup>2</sup> is not H or Me if n is 0 and R<sup>1</sup> is Me] are prepd. by an Arbusev reaction of

R<sup>1</sup>(XCH<sub>2</sub>CH<sub>2</sub>)<sub>n</sub>OCHCl<sub>2</sub>

(II) with P(OR<sub>3</sub>)<sub>3</sub> (R<sub>3</sub> = C<sub>1</sub>-6 alkyl), treatment of the product with NaPO(OR<sub>3</sub>)<sub>2</sub> (III), and ester cleavage of the resulting compds., with optional alkylation or halogenation, to give I. Alternatively, II may be reacted with 2 equivs. of the phosphite or of III, followed by ester cleavage etc. Salts and readily hydrolyzed (in vivo) esters of I are also

claimed. These compds. are useful for the treatment of arthritic disorders, atherosclerosis, and disorders involving Ca imbalance. Thus, BuOCHCl<sub>2</sub>P(O)(OEt)<sub>2</sub> was prepd. by reaction of BuOCHCl<sub>2</sub> with P(OEt)<sub>3</sub>, and was

treated with III (R<sub>3</sub> = Et) to give the tetra-Et ester of I (R<sup>1</sup> = Bu, R<sup>2</sup> = H, n = 0). The ester was converted to the tris(benzylamine) salt, which was tested by s.c. administration to female rats, and showed good inhibition of bone resorption, as measured by hydroxyproline excretion. PhOCH(PO<sub>3</sub>HNa)<sub>2</sub> (50 g) was combined with NaCl (60 g), NaOAc (20 g), HOAc, and water to 10000 mL, to give a sterile soln. of pH 5.2 for injection.

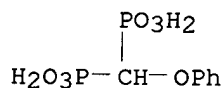
IT 104392-52-1P 104407-76-3P 104407-80-9P  
104407-92-3P 104407-93-4P 104407-94-5P  
104407-96-7P 104407-97-8P 104426-62-2P  
105810-40-0P

RL: SPN (Synthetic preparation); **PREP (Preparation)**

(prepn. of, for arthritis and calcium-metab. therapy)

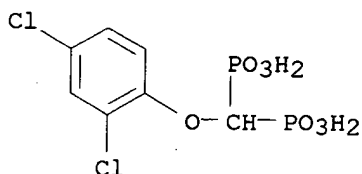
RN 104392-52-1 CAPLUS

CN Phosphonic acid, (phoxymethylene)bis- (9CI) (CA INDEX NAME)



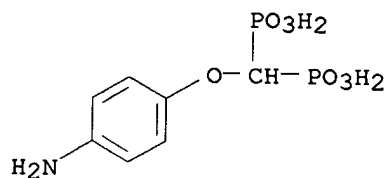
RN 104407-76-3 CAPLUS

CN Phosphonic acid, [(2,4-dichlorophenoxy)methylene]bis- (9CI) (CA INDEX NAME)



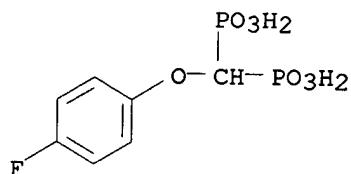
RN 104407-80-9 CAPLUS

CN Phosphonic acid, [(4-aminophenoxy)methylene]bis- (9CI) (CA INDEX NAME)



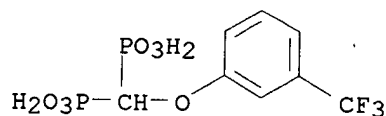
RN 104407-92-3 CAPLUS

CN Phosphonic acid, [(4-fluorophenoxy)methylene]bis- (9CI) (CA INDEX NAME)



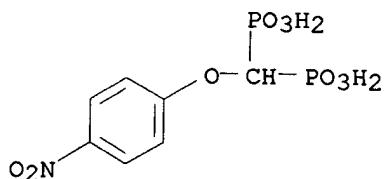
RN 104407-93-4 CAPLUS

CN Phosphonic acid, [[3-(trifluoromethyl)phenoxy]methylene]bis- (9CI) (CA INDEX NAME)



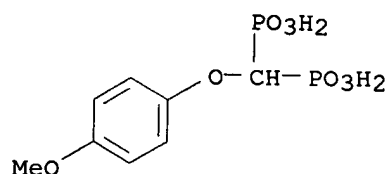
RN 104407-94-5 CAPLUS

CN Phosphonic acid, [(4-nitrophenoxy)methylene]bis- (9CI) (CA INDEX NAME)

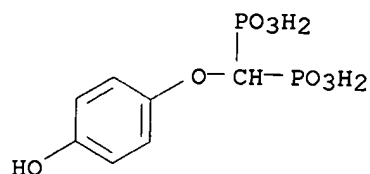


RN 104407-96-7 CAPLUS

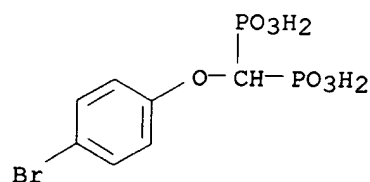
CN Phosphonic acid, [(4-methoxyphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



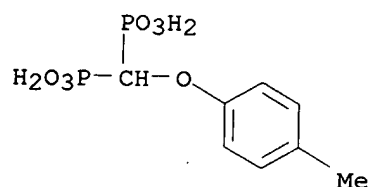
RN 104407-97-8 CAPLUS  
 CN Phosphonic acid, [(4-hydroxyphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



RN 104426-62-2 CAPLUS  
 CN Phosphonic acid, [(4-bromophenoxy)methylene]bis- (9CI) (CA INDEX NAME)



RN 105810-40-0 CAPLUS  
 CN Phosphonic acid, [(4-methylphenoxy)methylene]bis- (9CI) (CA INDEX NAME)



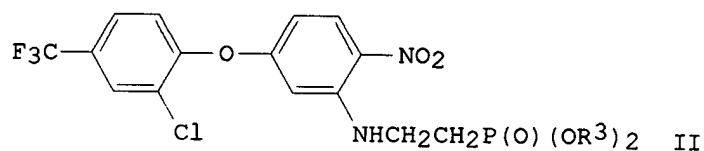
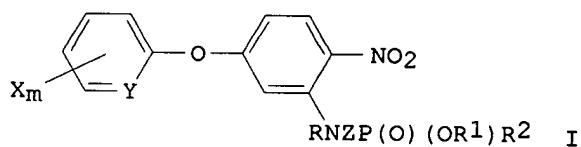
L18 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1984:121357 CAPLUS  
 DOCUMENT NUMBER: 100:121357  
 TITLE: (2-Nitro-5-aryloxyphenylamino)alkylphosphonic,  
 -phosphinic and phosphinous acid derivatives useful  
 as herbicides and plant growth regulators  
 INVENTOR(S): Maier, Ludwig  
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G. , Switz.



SOURCE: Eur. Pat. Appl., 39 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 93081	A2	19831102	EP 1983-810157	19830418
EP 93081	A3	19840328		
EP 93081	B1	19860319		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL				
AT 18670	E	19860415	AT 1983-810157	19830418
IL 68452	A1	19860831	IL 1983-68452	19830421
ES 521763	A1	19840701	ES 1983-521763	19830422
JP 58194893	A2	19831112	JP 1983-72048	19830423
US 4618358	A	19861021	US 1984-651968	19840919
PRIORITY APPLN. INFO.:				
			CH 1982-2500	19820423
			CH 1982-6585	19821111
			US 1983-484765	19830414
			EP 1983-810157	19830418

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AB Approx. 30 title compds. I (X = halo, NO<sub>2</sub>, CN, CONH<sub>2</sub>, CSNH<sub>2</sub>; Y = CH, N; Z = alkylene; R = H, C1-4 alkyl, aralkyl; R<sub>1</sub> = H, C1-4 alkyl, cation; R<sub>2</sub> = C1-4 alkyl, haloalkyl, alkoxy, OH, OM, M = cation) were prepd. by treating

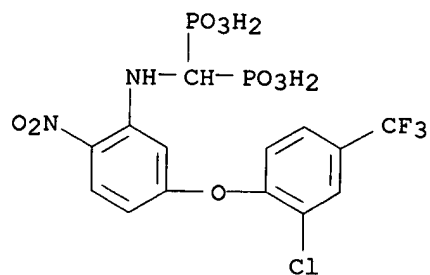
nitrophenyl ethers with aminoalkanephosphorus acid esters followed by hydrolysis. Thus, 0.064 mol 3,4-(O<sub>2</sub>N)2C<sub>6</sub>H<sub>3</sub>OC<sub>6</sub>H<sub>3</sub>(CF<sub>3</sub>)Cl-4,2 was refluxed in PhMe with 0.128 mol H<sub>2</sub>NCH<sub>2</sub>P(O)(OCHMe<sub>2</sub>)<sub>2</sub> to give 96% II (R<sub>3</sub> = CHMe<sub>2</sub>) (III), which was hydrolyzed to give 92% II (R = H). At 4 kg/ha III gave 100% kill of Salanum and Sinapis after 15 days.

IT **89175-56-4P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)

RN 89175-56-4 CAPLUS

CN Phosphonic acid, [[[5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrophenyl]amino]methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1984:23212 CAPLUS

DOCUMENT NUMBER: 100:23212

TITLE: Synthesis of ion-exchange resins with aminoalkylidenediphosphonate groups

AUTHOR(S): Petrov, K. A.; Chazov, V. A.; Pazhitnova, N. V.

CORPORATE SOURCE: USSR

SOURCE: Vysokomol. Soedin., Ser. B (1983), 25(10), 739-41  
CODEN: VYSBAI; ISSN: 0507-5483

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Ion exchanges with aminoalkylidenediphosphonate groups were prepd. by condensation of N-arylaminoalkylidenediphosphonic acids (I) in alk. media with HCHO and resorcinol or PhOH as crosslinking agent. The I monomers were prepd. by the reaction of acetanilide, formanilide, or m-phenylenebisformamide with a mixt. of PCl<sub>3</sub> and H<sub>3</sub>PO<sub>3</sub>. The ion exchange capacity (IEC) of the resins was 4.39-8.35 mg-equiv. NaOH/g. The

sorption

capacity of N-phenylaminomethylenediphosphonic acid-based and N-phenylaminoethylidenediphosphonic acid-based ion exchangers in H<sup>+</sup> form for Cu<sup>2+</sup> was 2.84 and 4.40 mg-equiv/g, resp. The higher IEC of the

resins

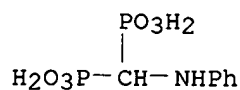
compared to their sorption capacity was due to the participation of phenolic OH groups in the ion exchange.

IT 54767-26-9P 88254-39-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, for ion exchanger manuf.)

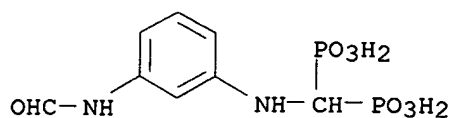
RN 54767-26-9 CAPLUS

CN Phosphonic acid, [(phenylamino)methylene]bis- (9CI) (CA INDEX NAME)



RN 88254-39-1 CAPLUS

CN Phosphonic acid, [[[3-(formylamino)phenyl]amino]methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1982:158356 CAPLUS

DOCUMENT NUMBER: 96:158356

TITLE: Studies for Tc-99m labeling ability of derivatives of the aminomethanediphosphonic acid

AUTHOR(S): Unterspann, S.; Finck, W.

CORPORATE SOURCE: Radiol. Klin., Wilhelm-Pieck-Univ. Rostock, Rostock, Ger. Dem. Rep.

SOURCE: Dtsch. Gesundheitswes. (1981), 36(52), 2205-10

CODEN: DEGEA3; ISSN: 0012-0219

DOCUMENT TYPE: Journal

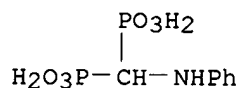
LANGUAGE: German

AB Aminomethanediphosphonic acid and 10 derivs. were labeled with 99mTc and were investigated in mice for bone scintigraphy. 99mTc-labeled methylaminomethanediphosphonate labeled bone to the greatest extent. The N-dimethylated and N-trimethylated derivs. were somewhat less effective than the N-monomethylated 1 but were more effective than 99mTc-labeled aminomethanediphosphonate. 99mTc-labeled butylaminomethanediphosphonate had relatively high affinity for bone. The 3 Ph contg. diphosphonates also were selectively incorporated by bone. 99mTc-labeled aminomethanediphosphonate itself was selectively incorporated by the liver.

IT **54767-26-9DP**, technetium-99 complexes **59611-67-5DP**, technetium-99 complexes **59611-70-0DP**, technetium-99 complexes  
 RL: BPR (Biological process); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; PROC (Process)  
 (prepn. and metab. of, bone scintigraphy in relation to)

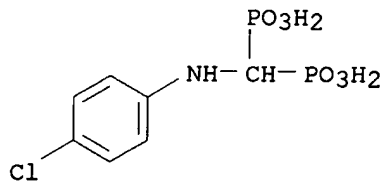
RN 54767-26-9 CAPLUS

CN Phosphonic acid, [(phenylamino)methylene]bis- (9CI) (CA INDEX NAME)

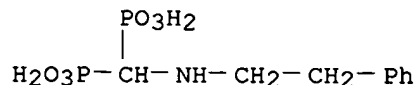


RN 59611-67-5 CAPLUS

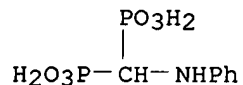
CN Phosphonic acid, [[(4-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



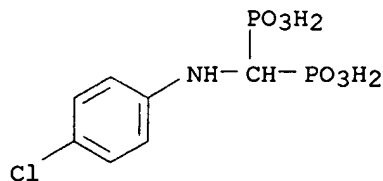
RN 59611-70-0 CAPLUS  
 CN Phosphonic acid, [[(2-phenylethyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



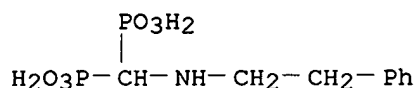
L18 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1982:64954 CAPLUS  
 DOCUMENT NUMBER: 96:64954  
 TITLE: Chemical structure and pharmacokinetics of technetium-99M-labeled aminomethane diphosphonic acid derivatives  
 AUTHOR(S): Unterspann, Siegfried; Finck, Wilhelm  
 CORPORATE SOURCE: Dep. Nucl. Med., Wilhelm-Pieck-Univ., Rostock, DDR-25,  
 Ger. Dem. Rep.  
 SOURCE: Eur. J. Nucl. Med. (1981), 6(11), 527-30  
 CODEN: EJNMD9; ISSN: 0340-6997  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 99mTc-labeled derivs. of aminomethane diphosphonic acid, as well as hydroxyethane diphosphonic acid and hydroxypropane monophosphonic acid, were investigated with regard to their suitability for skeleton scintigraphy. Bone accumulation in male rats was related to chem. structure. Compds. able to form enols were accumulated to a higher degree, and large substituents neg. influenced the affinity to bone due to steric hindrance.  
 IT **54767-26-9DP**, technetium-99 complexes **59611-67-5DP**, technetium-99 complexes **59611-70-0DP**, technetium-99 complexes  
 RL: BPR (Biological process); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**; PROC (Process)  
 (prepn. and metab. of, bone scintigraphy in relation to)  
 RN 54767-26-9 CAPLUS  
 CN Phosphonic acid, [(phenylamino)methylene]bis- (9CI) (CA INDEX NAME)



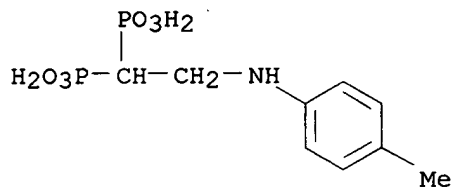
RN 59611-67-5 CAPLUS  
 CN Phosphonic acid, [[(4-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 59611-70-0 CAPLUS  
 CN Phosphonic acid, [[(2-phenylethyl)amino]methylene]bis- (9CI) (CA INDEX NAME)

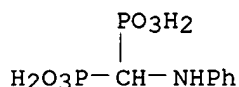


L18 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1980:639522 CAPLUS  
 DOCUMENT NUMBER: 93:239522  
 TITLE: Nucleophilic addition of amines to vinylidenediphosphonic acid  
 AUTHOR(S): Alfer'ev, I. S.; Kotlyarevskii, I. L.; Mikhalin, N. V.; Novikova, V. M.  
 CORPORATE SOURCE: Inst. Khim. Kinet. Gorennya, Novosibirsk, USSR  
 SOURCE: Izv. Akad. Nauk SSSR, Ser. Khim. (1980), (5), 1211-12  
 CODEN: IASKA6; ISSN: 0002-3353  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB Addn. of RR1NH to H2C:C[P(O)(OH)2]2 gave RR1NCH2CH[P(O)(OH)2]2 (R = Et, R1 = H; R = R1 = HOCH2CH2; R = HO2CCH2, R1 = H; RR1 = (CH2CH2)2O; R = p-tolyl, R1 = H).  
 IT 75669-56-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)  
 RN 75669-56-6 CAPLUS  
 CN Phosphonic acid, [2-[(4-methylphenyl)amino]ethylenediphosphonic acid]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1980:164036 CAPLUS

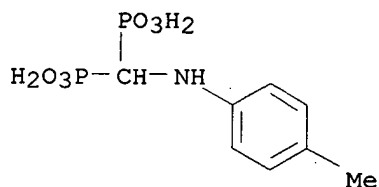
DOCUMENT NUMBER: 92:164036  
 TITLE: Reactions of 1-aminoalkane-1,1-diphosphonic acids with nitrous acid  
 AUTHOR(S): Worms, K. H.; Blum, H.  
 CORPORATE SOURCE: Henkel KGaA, Duesseldorf, D-4000/1, Fed. Rep. Ger.  
 SOURCE: Z. Anorg. Allg. Chem. (1979), 457, 209-13  
 CODEN: ZAACAB; ISSN: 0044-2313  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German  
 AB The reaction of  $\text{RC}(\text{NH}_2)[\text{P}(\text{O})(\text{OH})_2]_2$  with  $\text{HNO}_2$  gave 52-84%  $\text{RC}[\text{P}(\text{O})(\text{OH})_2]_2\text{OH}$  ( $\text{R} = \text{Ph}, \text{p-ClC}_6\text{H}_4, 3,4\text{-Me}_2\text{C}_6\text{H}_3, \text{p-HOC}_6\text{H}_4, \text{Me}, \text{Pr}, \text{cyclohexyl}$ ). In  $\text{HCl}$ , the reaction gave 76-83%  $\text{RC}[\text{P}(\text{O})(\text{OH})_2]_2\text{Cl}$  ( $\text{R} = \text{Ph}, \text{p-ClC}_6\text{H}_4, 3,4\text{-Me}_2\text{C}_6\text{H}_3$ ).  
 IT **54767-26-9P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); **PREP** (Preparation)  
 (prepn. and reaction with nitrous acid)  
 RN 54767-26-9 CAPLUS  
 CN Phosphonic acid, [(phenylamino)methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1980:146905 CAPLUS  
 DOCUMENT NUMBER: 92:146905  
 TITLE: N-Substituted aminomethylenediphosphonic acids  
 INVENTOR(S): Suzuki, Fumio; Fujikawa, Yoshihiro; Yamamoto, Susumu; Mizutani, Hideyoshi; Iwasawa, Yoshihiro  
 PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	JP 54135724	A2	19791022	JP 1978-42349	19780411
AB	Six aminomethylenediphosphonic acids, $\text{RR1NCH}[\text{PO}(\text{OH})_2]_2$ [I, $\text{RR1N} = \text{p-toluidino}, \text{pyrimidin-2-ylamino}, \text{n-C}_8\text{H}_{17}\text{NH}, 4\text{-methylpiperidin-1-yl}, (\text{CH}_2:\text{CHCH}_2)_2\text{N}, 3\text{-methylpyrazolin-5-ylamino}$ ] were prepd. by heating $\text{RR1NH}$ with $\text{HC}(\text{OEt})_3$ and $(\text{EtO})_2\text{POH}$ , followed by hydrolysis of the resulting $\text{RR1NCH}[\text{PO}(\text{OEt})_2]_2$ (II). Thus, 5.3 g p-toluidine heated with 9.25 g $\text{HC}(\text{OEt})_3$ and 13.8 g $(\text{EtO})_2\text{POH}$ at 150.degree. 1 h gave 20 g II ( $\text{RR1N} = \text{p-toluidino}$ ), which (5 g) was heated with 10 mL concd. $\text{HCl}$ 2 h to give				
2.1	g I ( $\text{RR1N} = \text{p-toluidino}$ ).				
IT	<b>73269-57-5P</b>				

RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)  
 RN 73269-57-5 CAPLUS  
 CN Phosphonic acid, [[(4-methylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)

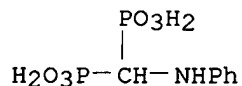


L18 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1979:557893 CAPLUS  
 DOCUMENT NUMBER: 91:157893  
 TITLE: 1-Aminoalkane-1,1-diphosphonic acids  
 INVENTOR(S): Sommer, Klaus  
 PATENT ASSIGNEE(S): Benckiser-Knapsack G.m.b.H., Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 14 pp. Addn. to Ger. Offen. 2,625,767.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	DE 2754821	A1	19790613	DE 1977-2754821	19771209
	DE 2754821	B2	19810108		
	DE 2754821	C3	19810813		

AB Addn. of HP(O)(OH)2 to RCN gave 15 RC(NH2)[P(O)(OH)2]2. Thus, PhCN and HP(O)(OH)2 in the presence of AlCl3 or AlBr3 at 150.degree. gave 72.6% PhC(NH2)[P(O)(OH)2]2.

IT **54767-26-9P**  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)  
 RN 54767-26-9 CAPLUS  
 CN Phosphonic acid, [(phenylamino)methylene]bis- (9CI) (CA INDEX NAME)



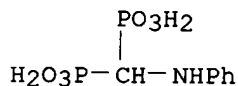
L18 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1976:433126 CAPLUS  
 DOCUMENT NUMBER: 85:33126  
 TITLE: .alpha.-Substituted phosphonates. XIX. Derivatives of aminomethanebisphosphonic acid

AUTHOR(S): Gross, H.; Costisella, B.; Gnauk, T.; Brennecke, L.  
 CORPORATE SOURCE: Zentralinst. Org. Chem., DAW, Berlin-Adlershof, E. Ger.  
 SOURCE: J. Prakt. Chem. (1976), 318(1), 116-26  
 CODEN: JPCEAO  
 DOCUMENT TYPE: Journal  
 LANGUAGE: German

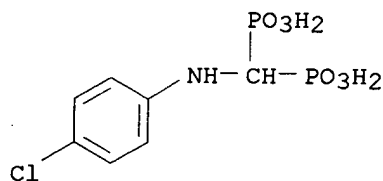
AB R1R2NCR[P(O)(OEt)2]2 (I) were prep'd. by several methods. E.g.,  
 R1R2NCR(OMe)2 and HP(O)(OEt)2 gave 40-42% I [R = H, R1 = Me, R2 = PhCH2  
 (II), R1 = R2 = Me (III), R1R2 = (CH2)5 (IV), (CH2)2O(CH2)2 (V)].  
 R1R2N+:CRCl Cl- and P(OEt)2 gave 30-76% II-V and I [R = Ph, p-O2NC6H4,  
 3,5-(O2N)2C6H3, R1R2 = (CH2)5]. R1N:C[P(O)(OEt)2]2 were hydrogenated  
 with NaBH4 to give 70-81% I (R = R2 = H, R1 = Ph, o-, p-ClC6H4, m-O2NC6H4,  
 p-EtO2CC6H4). The aminomethanebisphosphonates prep'd. were hydrolyzed to  
 give the phosphonic acids. E.g., hydrolysis of I gave 72-93%  
 R1R2NCH[P(O)(OH)2]2 [R1 = R2 = Me, R1R2 = (CH2)5, (CH2)2O(CH2)2, R1 = Ph,  
 o-, p-ClC6H4, p-HO2CC6H4, R2 = H].

IT 54767-26-9P 59611-67-5P 59611-68-6P  
 59611-69-7P 59611-70-0P  
 RL: SPN (Synthetic preparation); **PREP (Preparation)**  
 (prepn. of)

RN 54767-26-9 CAPLUS  
 CN Phosphonic acid, [(phenylamino)methylene]bis- (9CI) (CA INDEX NAME)

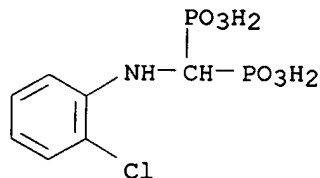


RN 59611-67-5 CAPLUS  
 CN Phosphonic acid, [[(4-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)

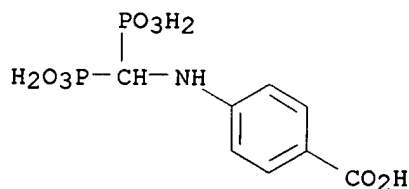


RN 59611-68-6 CAPLUS  
 CN Phosphonic acid, [[(2-chlorophenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)

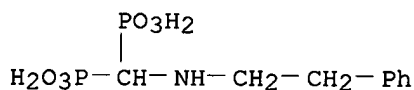




RN 59611-69-7 CAPLUS  
 CN Benzoic acid, 4-[(diphosphonomethyl)amino]- (9CI) (CA INDEX NAME)



RN 59611-70-0 CAPLUS  
 CN Phosphonic acid, [[(2-phenylethyl)amino]methylen]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1972:434645 CAPLUS

DOCUMENT NUMBER: 77:34645

TITLE: Preparation of 1-aminoalkylidenediphosphonic acids

AUTHOR(S): Ploeger, W.; Schindler, N.; Wollmann, K.; Worms, K. H.

CORPORATE SOURCE: Henkel und Cie. G.m.b.H., Duesseldorf, Ger.

SOURCE: Z. Anorg. Allg. Chem. (1972), 389(2), 119-28

CODEN: ZAACAB

DOCUMENT TYPE: Journal

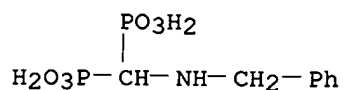
LANGUAGE: German

AB Title compds. [(HO)2P(O)]2C(R)N(R1)R2 [I; R = H, C1-15 alkyl, HO2CCH2, Ph,

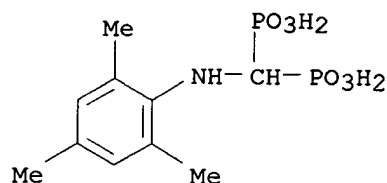
PhCH2, or PhCH2CH2; R1 = H or C1-18 alkyl; R2 = H, C1-18 alkyl, cyclohexyl, PhCH2, 2,4,6-Me3C6H2, or 4-pyridyl; or N(R1)R2 = piperidino or

morpholino] were prepd. in 13-78% yield by reaction of H3PO3 with R2(R1)N+:C(R)XCl- (X = Cl or OH), or from PCl3-H2O and RCON(R1)R2. Reaction of HCONH2 (II) with PCl3 and H3PO3 in 1:3:1 molar ratio 1 hr at 70.degree. and hydrolysis yielded 30% (based on II) I (R = R1 = R2 = H), whereas on reaction of II with PCl3 in 1:0.33 molar ratio 2 hr at 60.degree. and hydrolysis 30% (based on PCl3) 5-amino-2-hydroxy-1,4,2-oxazaphospholidine-3-phosphonic acid 2-oxide was obtained.

IT 32545-71-4P 37634-97-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 32545-71-4 CAPLUS  
 CN Phosphonic acid, [[(phenylmethyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



RN 37634-97-2 CAPLUS  
 CN Phosphonic acid, [[(2,4,6-trimethylphenyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



L18 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1971:436335 CAPLUS  
 DOCUMENT NUMBER: 75:36335  
 TITLE: 1-Aminoalkane-1,1-diphosphonic acids  
 INVENTOR(S): Wollmann, Klaus; Ploeger, Walter; Worms, Karl H.  
 PATENT ASSIGNEE(S): Henkel und Cie. G.m.b.H.  
 SOURCE: Ger. Offen., 28 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1958123	A	19710519	DE 1969-1958123	19691119
DE 1958123	C3	19780928		
NL 7015156	A	19710524	NL 1970-15156	19701015
NL 167700	B	19810817		
NL 167700	C	19820118		
SE 373371	B	19750203	SE 1970-13950	19701015
US 3846420	A	19741105	US 1970-90454	19701117
GB 1267016	A	19720315	GB 1970-1267016	19701118
ES 385658	A1	19730316	ES 1970-385658	19701118
CH 540935	A	19731015	CH 1970-17086	19701118
FR 2069656	A5	19710903	FR 1970-41475	19701119
JP 49014733	B4	19740410	JP 1970-101890	19701119
US 3979385	A	19760907	US 1974-475207	19740531

## PRIORITY APPLN. INFO.:

DE 1969-1958123 19691119

US 1970-90454 19701117

AB The title compds.  $\text{RR}_1\text{N}(\text{CH}_2)_n\text{CH}(\text{PO}_3\text{H}_2)_2$  (I) with complexing properties, useful for water softening or as intermediates for detergents, were

prepd.

by reaction of P trihalides with carboxamides. Among .apprx.20 compds. prepd. were I (R,  $\text{R}_1$ , and n given): Me, Me, 0; Me, H, 1; Bu, Bu, 0,

$\text{PhCH}_2$ ,

H, 0; n-C<sub>18</sub>H<sub>37</sub>, n-C<sub>18</sub>H<sub>37</sub>, 0.

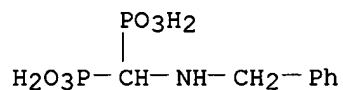
IT **32545-71-4P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**

(prepn. of)

RN 32545-71-4 CAPLUS

CN Phosphonic acid, [[(phenylmethyl)amino]methylene]bis- (9CI) (CA INDEX NAME)



=> s (hiv or aids) (1) tissue factor inhibition

```

36392 HIV
  67 HIVS
36397 HIV
      (HIV OR HIVS)
32227 AIDS
421332 TISSUE
206793 TISSUES
538748 TISSUE
      (TISSUE OR TISSUES)
591918 FACTOR
475023 FACTORS
909803 FACTOR
      (FACTOR OR FACTORS)
555060 INHIBITION
  3562 INHIBITIONS
556165 INHIBITION
      (INHIBITION OR INHIBITIONS)
  21 TISSUE FACTOR INHIBITION
      (TISSUE(W) FACTOR(W) INHIBITION)
L1      0 (HIV OR AIDS) (L) TISSUE FACTOR INHIBITION

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=> s tissue factor inhibit?

```

421332 TISSUE
206793 TISSUES
538748 TISSUE
      (TISSUE OR TISSUES)
591918 FACTOR
475023 FACTORS
909803 FACTOR
      (FACTOR OR FACTORS)
1262146 INHIBIT?
L2      95 TISSUE FACTOR INHIBIT?
      (TISSUE(W) FACTOR(W) INHIBIT?)

```

=> s 12 and (aids or hiv or human immun?)

```

32227 AIDS
36392 HIV
  67 HIVS
36397 HIV
      (HIV OR HIVS)
837840 HUMAN
267008 HUMANS
977376 HUMAN
      (HUMAN OR HUMANS)
556028 IMMUN?
  39514 IG
  11059 IGS
  44503 IG
      (IG OR IGS)

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566300 IMMUN?
      (IMMUN? OR IG)
38533 HUMAN IMMUN?
      (HUMAN(W)IMMUN?)
L3      0 L2 AND (AIDS OR HIV OR HUMAN IMMUN?)

=> s tf inhibit?

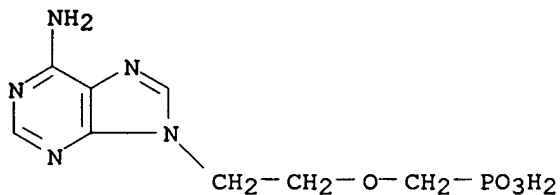
      7530 TF
      304 TFS
      7736 TF
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1262146 INHIBIT?
L4      26 TF INHIBIT?
      (TF(W)INHIBIT?)

=> s l4 (l) (hiv or aids)

      36392 HIV
      67 HIVS
      36397 HIV
      (HIV OR HIVS)
      32227 AIDS
L5      0 L4 (L) (HIV OR AIDS)

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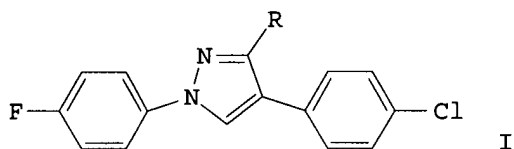
ACCESSION NUMBER: 1997:282633 CAPLUS  
 DOCUMENT NUMBER: 126:324966  
 TITLE: Attempts to use liposomes and RBC ghosts as vectors  
 in drug and antisense therapy of virus infection  
 AUTHOR(S): Grimaldi, S.; Lisi, A.; Pozzi, D.; Santoro, N.  
 CORPORATE SOURCE: Istituto di Medicina Sperimentale C.N.R., Rome,  
 00137, Italy  
 SOURCE: Res. Virol. (1997), 148(2), 177-180  
 CODEN: RESVEY; ISSN: 0923-2516  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Selective targeting of drugs or oligonucleotide for the treatment  
 of viral diseases or cancer is the objective of new strategies  
 that pursue therapy optimization and redn. of toxicity. In this work we  
 report two protocols based on encapsulation of anti-human  
 immunodeficiency virus drugs within targeted liposomes or erythrocytes. Both have been  
 shown to be effective for the specific delivery of drugs or  
 oligonucleotide in the treatment of viral infection.  
 Liposome-mediated antisense transfer is briefly reviewed.  
 IT 106941-25-7, PMEA  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibition of HIV-1 in macrophages with PMEA encapsulated in  
 erythrocytes or liposomes)  
 RN 106941-25-7 CAPLUS  
 CN Phosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]- (9CI) (CA  
 INDEX NAME)



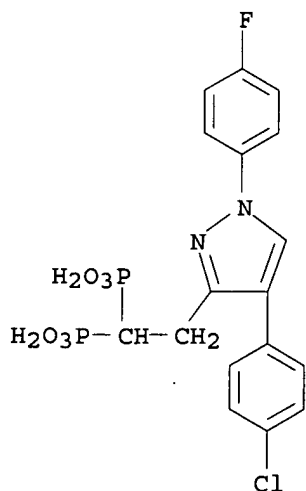
ACCESSION NUMBER: 1983:612705 CAPLUS  
 DOCUMENT NUMBER: 99:212705  
 TITLE: Antiinflammatory and antiarthritic  
 pyrazolyethanephosphonates.  
 INVENTOR(S): Biere, Helmut; Rufer, Clemens; Boettcher, Irmgard  
 PATENT ASSIGNEE(S): Schering A.-G. , Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 19 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3203307	A1	19830728	DE 1982-3203307	19820127

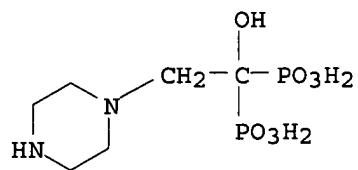
OTHER SOURCE(S): CASREACT 99:212705  
 GI



AB Approx. 20 title compds. I [R = CH:C(OH)P(O)(OEt)<sub>2</sub> (II), CH<sub>2</sub>CH(OH)P(O)(ONa)<sub>2</sub>, CH<sub>2</sub>C(NH<sub>2</sub>)P(O)(OH)<sub>2</sub>, etc.] were prepd. Thus, 17.5 g 4-(p-chlorophenyl)-1-(p-fluorophenyl)-3-pyrazoleacetyl chloride in 100 mL THF was treated with 9.8 mL P(OEt)<sub>3</sub> to give 83.4% II, which was hydrolyzed to give 74.2% I [R = CH:C(OH)P(O)(OH)<sub>2</sub>].  
 IT **87965-46-6P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 87965-46-6 CAPLUS  
 CN Phosphonic acid, [2-[4-(4-chlorophenyl)-1-(4-fluorophenyl)-1H-pyrazol-3-yl]ethylidene]bis- (9CI) (CA INDEX NAME)

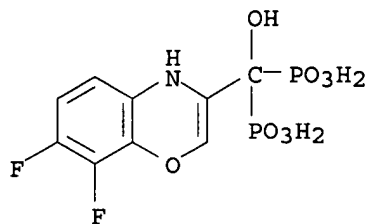


IN Phosphonic acid, [1-hydroxy-2-(1-piperazinyl)ethylidene]bis- (9CI)  
MF C6 H16 N2 O7 P2

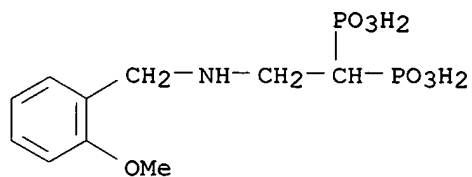




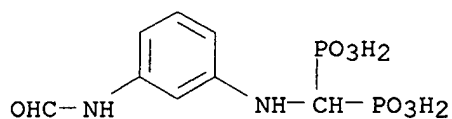
IN Phosphonic acid, [(7,8-difluoro-4H-1,4-benzoxazin-3-  
yl)hydroxymethylene]bis- (9CI)  
MF C9 H9 F2 N O8 P2



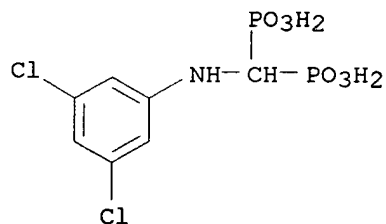
IN Phosphonic acid, [2-[(2-methoxyphenyl)methyl]amino]ethylidene]bis- (9CI)  
 MF C10 H17 N O7 P2



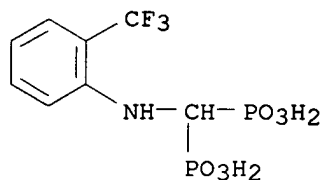
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [[[3-(formylamino)phenyl]amino]methylene]bis- (9CI)  
 MF C8 H12 N2 O7 P2  
 CI COM



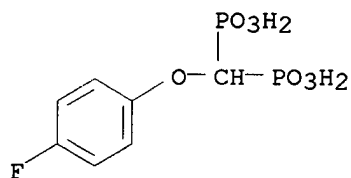
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [[[3,5-dichlorophenyl]amino]methylene]bis- (9CI)  
 MF C7 H9 Cl2 N O6 P2



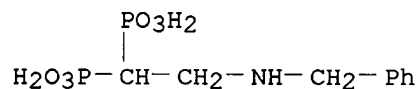
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [[[2-(trifluoromethyl)phenyl]amino]methylene]bis- (9CI)  
 MF C8 H10 F3 N O6 P2



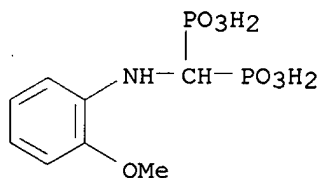
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [(4-fluorophenoxy)methylene]bis- (9CI)  
 MF C7 H9 F O7 P2



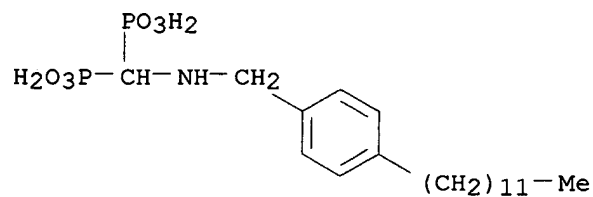
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [2-[(phenylmethyl)amino]ethylidene]bis- (9CI)  
 MF C9 H15 N O6 P2



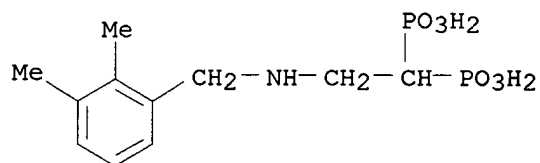
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [[(2-methoxyphenyl)amino]methylene]bis- (9CI)  
 MF C8 H13 N O7 P2



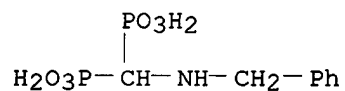
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [[[4-dodecylphenyl)methyl]amino]methylene]bis- (9CI)  
 MF C20 H37 N O6 P2



L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [2-[[ (2,3-dimethylphenyl)methyl]amino]ethylidene]bis-  
 (9CI)  
 MF C11 H19 N O6 P2



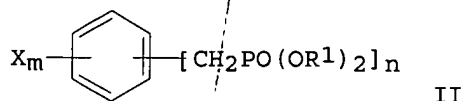
L14 83 ANSWERS REGISTRY COPYRIGHT 2000 ACS  
 IN Phosphonic acid, [[ (phenylmethyl)amino]methylene]bis- (9CI)  
 MF C8 H13 N O6 P2



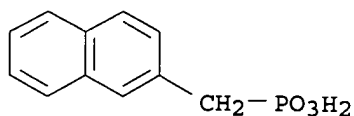
ACCESSION NUMBER: 1994:579868 CAPLUS  
 DOCUMENT NUMBER: 121:179868  
 TITLE: Preparation of arylmethylphosphonates and phosphonic acids useful as anti-inflammatory agents  
 INVENTOR(S): Johnson, Roy A.  
 PATENT ASSIGNEE(S): Upjohn Co., USA  
 SOURCE: PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9407501	A1	19940414	WO 1993-US8353	19930910
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 661978	A1	19950712	EP 1993-921363	19930910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08501794	T2	19960227	JP 1993-509064	19930910
PRIORITY APPLN. INFO.:				
			US 1992-949738	19920923
			US 1992-954093	19920930
			US 1992-964618	19921022
			US 1993-65056	19930520
			WO 1993-US8353	19930910

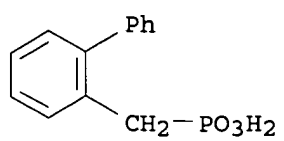
OTHER SOURCE(S): MARPAT 121:179868  
 GI



AB Title compds. ARCHXPO(R1O)2 (I; R1 = Na, K, H4N, C1-10 alkyl, PhCH2, Ph, etc.; Ar = (substituted) 1-, 2-naphthyl, 2-, 3-, 4-pyridyl, 1-, 2-, 9-anthryl, phenanthryl, substituted Ph; X = H, HO, Br, Cl, F) and II (M = 2,3; n = 3,4), are prepd. 2-(Bromomethyl)naphthalene and P(MeO)3 in MePH were refluxed for 144 h to give I (R = 2-naphthyl, X = H, R1 = Me) (III). III suppressed delayed-type hypersensitivity granuloma in mice at 10 mg/kg orally, by 54 and 50% (wet and dry wt.), resp.  
 IT 16672-84-7P 92025-82-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as antiinflammatory agent)  
 RN 16672-84-7 CAPLUS  
 CN Phosphonic acid, (2-naphthalenylmethyl)- (9CI) (CA INDEX NAME)



RN 92025-82-6 CAPLUS  
 CN Phosphonic acid, ([1,1'-biphenyl]-2-ylmethyl)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1995:632064 CAPLUS  
 DOCUMENT NUMBER: 123:33653  
 TITLE: Preparation of (phosphonoalkyl)peptide derivatives as inhibitors of endothelin converting enzyme.  
 INVENTOR(S): Ishikawa, Kiyofumi; Jukami, Takehiro; Hayama, Takashi; Matsuyama, Kenji; Noguchi, Kazuhito; Yano, Mitauo  
 PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan  
 SOURCE: Eur. Pat. Appl., 24 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 623625	A1	19941109	EP 1993-107203	19930504

R: CH, DE, FR, GB, IT, LI, NL

OTHER SOURCE(S): MARPAT 123:33653

AB H2O3PCH[(CH2)nR1]NHCHR2COAOH [n = 2, 3; R1 = H, (substituted) Ph, naphthyl, indolyl, benzothienyl, benzofuryl, benzoxazolyl; R2 = alkyl, benzyl, 4-hydroxybenzyl, 3-indolylmethyl, .beta.-phenethyl; A = Trp, Tyr, Phe, homoPhe, .alpha.-naphthylalanyl, N.omega.-nitroarginyl], were prepd. Thus, a mixt. of H-Leu-Trp-OBzl and PhCH2CH2CHO was refluxed 2 h in a Dean-Stark app.; dibenzyl phosphite and MeCN were added to the mixt. which was stirred at 80.degree. for 19 h to give N-[N-(1-dibenzyloxyphosphoryl-3-phenylpropyl)leucyl]tryptophan benzyl ester as a mixt. of diastereomers. The diastereomers were sep. hydrogenolyzed to give, after treatment with KOH, tripotassium N-[N-(3-phenyl-1-phosphonopropyl)leucyl]tryptophan diastereomers. One of the diastereomers at 10 .mu.M showed 88% inhibition of endothelin converting enzyme.

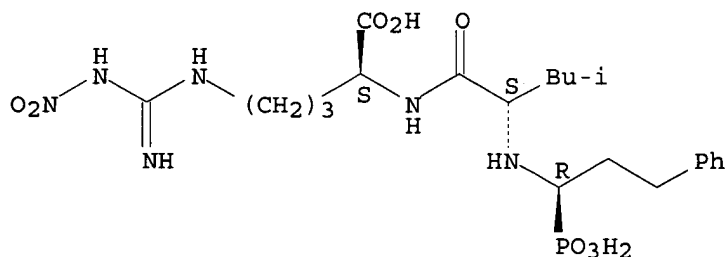
IT 164061-30-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

RN 164061-30-7 CAPLUS

CN L-Ornithine, N5-[imino(nitroamino)methyl]-N2-[N-(3-phenyl-1-phosphonopropyl)-L-leucyl]-, (R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT Antidiabetics and Hypoglycemics  
 Antihypertensives

(prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Thromboangiitis obliterans

(treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Blood vessel, disease

(Raynaud's phenomenon, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Heart, disease  
(angina pectoris, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Bronchodilators  
(antiasthmatics, prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Antiarteriosclerotics  
(antiatherosclerotics, prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Artery, disease  
(aortic arch syndrome, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Brain, disease  
(cerebrum, vasospasm, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Peptides, preparation  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(di-, prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Lymph node  
(disease, mucocutaneous lymph node syndrome, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Organ  
(disease, multiple organ failure, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT **Blood coagulation**  
(disorder, disseminated intravascular, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Shock  
(endotoxin, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Heart, disease  
(failure, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Kidney, disease  
(failure, acute, prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Brain, disease  
Heart, disease  
(infarction, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Intestine, disease  
(inflammatory, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT Heart, disease  
(restenosis, treatment; prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT 152290-30-7P  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT 152290-31-8P 152290-32-9P 152290-33-0P 152290-34-1P 152290-35-2P  
152290-36-3P 152290-38-5P 152290-39-6P 152376-06-2P 152376-07-3P  
152376-08-4P 152376-09-5P 152376-10-8P 152376-11-9P 152376-12-0P  
152376-14-2P 152376-15-3P 164061-29-4P **164061-30-7P**  
164061-39-6P 164202-33-9P 164202-34-0P 164202-40-8P 164202-41-9P  
164202-42-0P 164202-43-1P 164202-44-2P 164202-45-3P



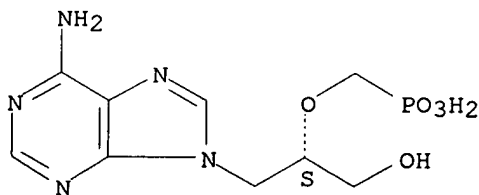
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

IT 138238-81-0, Endothelin converting enzyme

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(prepn. of (phosphonolalkyl)peptide derivs. as inhibitors of endothelin converting enzyme)

ACCESSION NUMBER: 1994:692044 CAPLUS  
 DOCUMENT NUMBER: 121:292044  
 TITLE: Dipyridamole potentiates the activity of various  
 acyclic nucleoside phosphonates against  
 human varicella-zoster virus, herpes simplex virus and  
 cytomegalovirus  
 AUTHOR(S): Snoeck, R.; Adrei, G.; Balzarini, J.; Reymen, D.; De  
 Clercq, E.  
 CORPORATE SOURCE: Rega Inst. Med. Res., Katholieke Univ. Leuven,  
 Louvain, B-3000, Belg.  
 SOURCE: Antiviral Chem. Chemother. (1994), 5(5), 312-21  
 CODEN: ACCHEH; ISSN: 0956-3202  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Dipyridamole (DPM) is widely used in the treatment of  
 cardiovascular diseases as a coronary vasodilator and inhibitor of  
 platelet aggregation. Phosphonylmethoxyethyl (PME) and  
 3-hydroxy-2-phosphonyl-methoxypropyl (HPMP) derivs. of purines and  
 pyrimidines are potent and selective inhibitors of varicella-zoster virus  
 (VZV), herpes simplex virus (HSV) and human cytomegalovirus (HCMV). We  
 have found that DPM markedly potentiates the antiviral effects of the PME  
 derivs. of adenine (PMEA) and 2,6-diaminopurine (PMEDAP), and of the HPMP  
 derivs. of adenine (HPMPA), 3-deazaadenine (HPMPc-3A) and cyclic HPMPA  
 (CHMPA). This was reflected by a significant decrease in the 50%  
 inhibitory concn. of the acyclic nucleoside phosphonates for VZV-, HSV-  
 and HCMV-induced cytopathic effect or plaque formation. DPM did not  
 enhance the activity of vidarabine, acyclovir or ganciclovir. These  
 results were confirmed by virus yield assays (for HSV and HCMV) and flow  
 cytometry (for VZV).  
 IT 92999-29-6, HPMPA  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dipyridamole potentiation of antiviral effect of hydroxy-phosphonyl-  
 methoxypropyl derivs. of adenine)  
 RN 92999-29-6 CAPLUS  
 CN Phosphonic acid, [[(1S)-2-(6-amino-9H-purin-9-yl)-1-  
 (hydroxymethyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

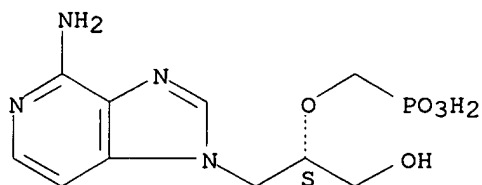
Absolute stereochemistry.



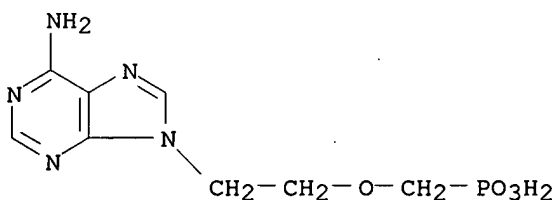
IT 128052-48-2D, 3-deazaadenine derivs.  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dipyridamole potentiation of antiviral effect of hydroxy-phosphonyl-  
 methoxypropyl derivs. of deazaadenine)

RN 128052-48-2 CAPLUS  
 CN Phosphonic acid, [[(S)-2-(4-amino-1H-imidazo[4,5-c]pyridin-1-yl)-1-(hydroxymethyl)ethoxy)methyl]- (9CI) (CA INDEX NAME)

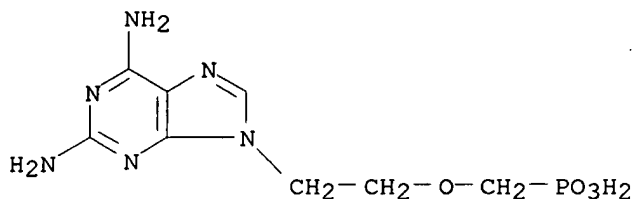
Absolute stereochemistry.



IT 106941-25-7, PMEAS  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dipyridamole potentiation of antiviral effect of phosphonylmethoxyethyl derivs. of adenine)  
 RN 106941-25-7 CAPLUS  
 CN Phosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]- (9CI) (CA INDEX NAME)



IT 113852-41-8, PMEDAP  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dipyridamole potentiation of antiviral effect of phosphonylmethoxyethyl derivs. of diaminopurine)  
 RN 113852-41-8 CAPLUS  
 CN Phosphonic acid, [[2-(2,6-diamino-9H-purin-9-yl)ethoxy)methyl]- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1994:692044 CAPLUS  
 DOCUMENT NUMBER: 121:292044  
 TITLE: Dipyridamole potentiates the activity of various  
 acyclic nucleoside phosphonates against  
 varicella-zoster virus, herpes simplex virus and  
 human cytomegalovirus  
 AUTHOR(S): Snoeck, R.; Adrei, G.; Balzarini, J.; Reymen, D.; De  
 Clercq, E.  
 CORPORATE SOURCE: Rega Inst. Med. Res., Katholieke Univ. Leuven,  
 Louvain, B-3000, Belg.  
 SOURCE: Antiviral Chem. Chemother. (1994), 5(5), 312-21  
 CODEN: ACCHEH; ISSN: 0956-3202  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Dipyridamole (DPM) is widely used in the **treatment** of  
**cardiovascular** diseases as a coronary vasodilator and inhibitor of  
 platelet aggregation. Phosphonylmethoxyethyl (PME) and  
 3-hydroxy-2-phosphonyl-methoxypropyl (HPMP) derivs. of purines and  
 pyrimidines are potent and selective inhibitors of varicella-zoster virus  
 (VZV), herpes simplex virus (HSV) and human cytomegalovirus (HCMV). We  
 have found that DPM markedly potentiates the antiviral effects of the PME  
 derivs. of adenine (PMEA) and 2,6-diaminopurine (PMEDAP), and of the HPMP  
 derivs. of adenine (HPMPA), 3-deazaadenine (HPMPc-3A) and cyclic HPMPA  
 (cHMPA). This was reflected by a significant decrease in the 50%  
 inhibitory concn. of the acyclic nucleoside phosphonates for VZV-, HSV-  
 and HCMV-induced cytopathic effect or plaque formation. DPM did not  
 enhance the activity of vidarabine, acyclovir or ganciclovir. These  
 results were confirmed by virus yield assays (for HSV and HCMV) and flow  
 cytometry (for VZV).

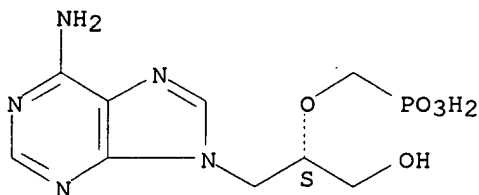
IT 92999-29-6, HPMPA

RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dipyridamole potentiation of antiviral effect of hydroxy-phosphonyl-  
 methoxypropyl derivs. of adenine)

RN 92999-29-6 CAPLUS

CN Phosphonic acid, [[(1S)-2-(6-amino-9H-purin-9-yl)-1-  
 (hydroxymethyl)ethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



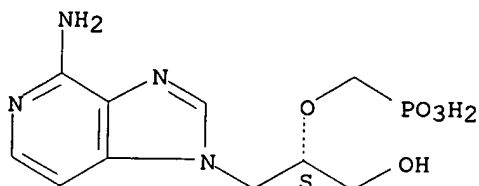
IT 128052-48-2D, 3-deazaadenine derivs.

RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dipyridamole potentiation of antiviral effect of hydroxy-phosphonyl-  
 methoxypropyl derivs. of deazaadenine)

RN 128052-48-2 CAPLUS

CN Phosphonic acid, [[(S)-2-(4-amino-1H-imidazo[4,5-c]pyridin-1-yl)-1-(hydroxymethyl)ethoxy)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

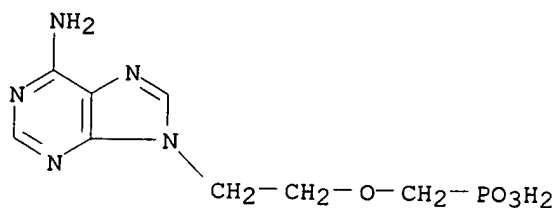


IT 106941-25-7, PMEAS

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dipyridamole potentiation of antiviral effect of phosphonylmethoxyethyl derivs. of adenine)

RN 106941-25-7 CAPLUS

CN Phosphonic acid, [[2-(6-amino-9H-purin-9-yl)ethoxy)methyl]- (9CI) (CA INDEX NAME)

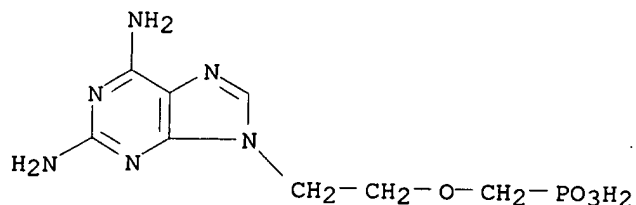


IT 113852-41-8, PMEDAP

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dipyridamole potentiation of antiviral effect of phosphonylmethoxyethyl derivs. of diaminopurine)

RN 113852-41-8 CAPLUS

CN Phosphonic acid, [[2-(2,6-diamino-9H-purin-9-yl)ethoxy)methyl]- (9CI) (CA INDEX NAME)





ACCESSION NUMBER: 1986:591393 CAPLUS  
 DOCUMENT NUMBER: 105:191393  
 TITLE: 2-Substituted-1,3-propylidenediphosphonate  
 derivatives  
 INVENTOR(S): and pharmaceutical compositions containing them  
 Nguyen Mong Lan; Niesor, Eric; Bentzen, Craig L.;  
 Guyon-Gellin, Yves; Kalathakis, Kyriacos; Phan Hieu  
 Trung; Rossier, Jean Robert  
 PATENT ASSIGNEE(S): Symphar S. A., Switz.  
 SOURCE: Eur. Pat. Appl., 134 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 173041	A1	19860305	EP 1985-108670	19850711
EP 173041	B1	19881130		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CH 664158	A	19880215	CH 1984-3488	19840718
AT 38991	E	19881215	AT 1985-108670	19850711
NO 8502822	A	19860120	NO 1985-2822	19850715
HU 38950	A2	19860728	HU 1985-2714	19850715
HU 193791	B	19871130		
IL 75807	A1	19890910	IL 1985-75807	19850715
ZA 8505357	A	19860226	ZA 1985-5357	19850716
US 4696920	A	19870929	US 1985-755712	19850716
FI 8502806	A	19860119	FI 1985-2806	19850717
FI 79327	B	19890831		
FI 79327	C	19891211		
DK 8503241	A	19860119	DK 1985-3241	19850717
AU 8545114	A1	19860123	AU 1985-45114	19850717
AU 581442	B2	19890223		
ES 545330	A1	19861216	ES 1985-545330	19850717
SU 1375141	A3	19880215	SU 1985-3926752	19850717
CS 262421	B2	19890314	CS 1985-5305	19850717
CA 1284320	A1	19910521	CA 1985-486929	19850717
JP 61040294	A2	19860226	JP 1985-157081	19850718
JP 05041155	B4	19930622		
CN 85106701	A	19870325	CN 1985-106701	19850905
CN 1009199	B	19900815		
PRIORITY APPLN. INFO.:			CH 1984-3488	19840718
			EP 1985-108670	19850711
<p>AB Title derivs. RCH[CH<sub>2</sub>P(O)(OR<sub>1</sub>)(OR<sub>2</sub>)]<sub>2</sub> [I; R = (un)substituted alkyl, aralkyl, etc.; R<sub>1</sub>, R<sub>2</sub> = H, metal ion, alkyl, etc.] are prepd. as slow Ca-channel inhibitors for treatment of cardiovascular conditions. Thus, PhOCH<sub>2</sub>CH<sub>2</sub>Br and NaCH(CO<sub>2</sub>Et)<sub>2</sub> reacted to give 72% PhOCH<sub>2</sub>CH<sub>2</sub>CH(CO<sub>2</sub>Et)<sub>2</sub>, which was reduced by LiAlH<sub>4</sub> to give 62% PhOCH<sub>2</sub>CH<sub>2</sub>CH(CH<sub>2</sub>OH)<sub>2</sub>. Tosylation of the diol gave 82% of the corresponding ditosylate, which reacted with NaP(O)(OBu)<sub>2</sub> to give 55-60% I (R = PhOCH<sub>2</sub>CH<sub>2</sub>, R<sub>1</sub> = R<sub>2</sub> = Bu) (II). At 1.0 .mu.M, II completely inhibited the binding of 3H-nitrendipine to homogenized rat cerebral membranes. I also</p>				

exhibited antihypertensive and muscle-relaxant activities. An exemplary gelatin capsule consisted of II 300, gelatin 100, glycerin 50, and K sorbate 0.5 mg/capsule.

IT 103486-15-3P

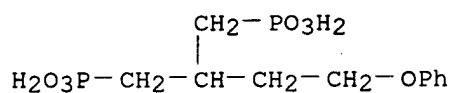
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as **cardiovascular** agent)

RN 103486-15-3 CAPLUS

CN Phosphonic acid, [2-(2-phenoxyethyl)-1,3-propanediyl]bis- (9CI) (CA

INDEX

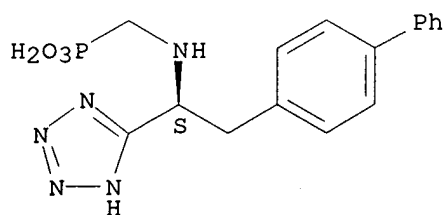
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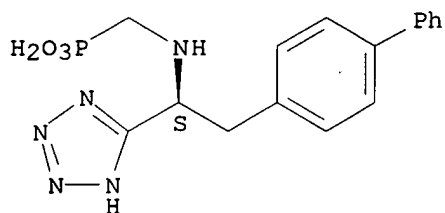
ACCESSION NUMBER: 1994:645784 CAPLUS  
 DOCUMENT NUMBER: 121:245784  
 TITLE: Pharmacological profile of a non-peptidic dual inhibitor of neutral endopeptidase 24.11 and endothelin-converting enzyme  
 AUTHOR(S): Lombaert, Stephane De; Ghai, Rajendra D.; Jeng, Arco Y.; Trapani, Angelo J.; Webb, Randy L.  
 CORPORATE SOURCE: Pharmaceuticals Div., CIBA-GEIGY Corp., Summit, NJ, 07901, USA  
 SOURCE: Biochem. Biophys. Res. Commun. (1994), 204(1), 407-12  
 CODEN: BBRCA9; ISSN: 0006-291X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB CGS 26303 is a potent and structurally unique non-peptidic inhibitor of neutral endopeptidase (NEP) capable of protecting atrial natriuretic peptide (ANP) from enzymic degrdn. In addn., CGS 26303 displays modest endothelin-converting enzyme (ECE) inhibitory activity in vitro. Unlike CGS 24592, a potent but selective NEP inhibitor, CGS 26303 significantly blocks endothelin-1 prodn. in rats after exogenous administration of big ET-1 and reduces and mean arterial pressure in spontaneously hypertensive rats during chronic administration. These results suggest that CGS 26303 represents a new class of therapeutic agents with potential benefits for the **treatment** of **cardiovascular** and renal disorders.  
 IT 154116-31-1, CGS 26303  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CGS 26303 represents a new class of antihypertensives which act as inhibitors of neutral endopeptidase 24.11 and endothelin-converting enzyme)  
 RN 154116-31-1 CAPLUS  
 CN Phosphonic acid, [[[1S)-2-[1,1'-biphenyl]-4-yl-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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 IT 154116-31-1, CGS 26303  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CGS 26303 represents a new class of antihypertensives which act as inhibitors of neutral endopeptidase 24.11 and endothelin-converting enzyme)  
 RN 154116-31-1 CAPLUS  
 CN Phosphonic acid, [[[1S)-2-[1,1'-biphenyl]-4-yl]-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1996:546615 CAPLUS  
 DOCUMENT NUMBER: 125:275882  
 TITLE: Phosphono-substituted tetrazole derivatives and  
 analogs as ECE inhibitors  
 INVENTOR(S): DeLombaert ,Stephane; Jeng, Arco Y.; Ksander, Gary M.  
 PATENT ASSIGNEE(S): Ciba-Geigy Corporation, USA  
 SOURCE: U.S., 25 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5550119	A	19960827	US 1995-403353	19950302
WO 9626729	A1	19960906	WO 1996-EP699	19960220
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AU 9648786	A1	19960918	AU 1996-48786	19960220
PRIORITY APPLN. INFO.:			US 1995-403353	19950302
			WO 1996-EP699	19960220

OTHER SOURCE(S): MARPAT 125:275882  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to N-(phosphonomethyl)-substituted compds. I [R0 = (CH2)nT, XCOR3; n = 0, 1, 2; T = 1H-tetrazol-5-yl; R, R' = H, aryl, 5-indanyl, 6-tetrahydronaphthyl, (un)substituted alkyl, etc.; R1 = (un)substituted Ph, thienyl, furanyl; or R1 = H when R0 = (CH2)nT; R2, R4 = H, alkyl, OH, alkoxy, halo, CF3; R3 = OH or acceptable ester group; X = bond, alkylene, alkenylene], and their pharmaceutically acceptable salts, as well as pharmaceutical compns., prepn. methods, and methods of use. For example, (S)-4-PhC6H4CH2CH(NH-Boc)CO2H [Boc = CO2Bu-tert] underwent amidation with H2NCH2CH2CN, and cyclocondensation with Me3SiN3 via Mitsunobu reaction, to give intermediate tetrazole deriv. II. This underwent deprotection of the Boc-amino group with CF3CO2H, N-alkylation with CF3SO2OCH2P(O)(OMe)2, deprotection of the tetrazole N with aq. NaOH, and hydrolysis of the phosphonate ester with aq. HCl in AcOH, to give title compd. III. In vitro tests of III for inhibition of porcine endothelin-converting enzyme (ECE) and human recombinant ECE gave IC50 values of 1.1 .mu.M and 0.1 .mu.M, resp.

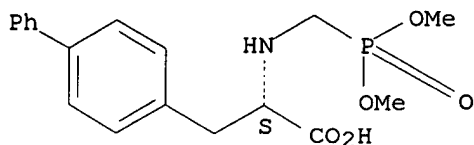
IT 147862-23-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (intermediate; prepn. of phosphono-substituted tetrazole derivs. and  
 analogs as ECE inhibitors)

RN 147862-23-5 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid,  
 .alpha.-[[ (dimethoxyphosphinyl)methyl]am  
 ino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 153037-39-9P 182192-87-6P

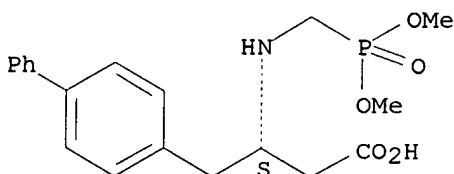
RL: BAC (Biological activity or effector, except adverse); RCT  
 (Reactant);

SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (product and intermediate; prepn. of phosphono-substituted tetrazole  
 derivs. and analogs as ECE inhibitors)

RN 153037-39-9 CAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid,  
 .beta.-[[ (dimethoxyphosphinyl)methyl]amin  
 o]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

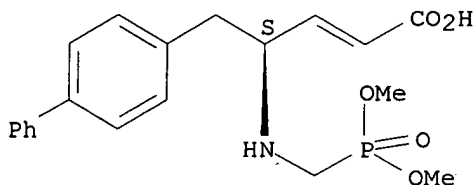


RN 182192-87-6 CAPLUS

CN 2-Pentenoic acid,  
 5-[1,1'-biphenyl]-4-yl-4-[[ (dimethoxyphosphinyl)methyl]a  
 mino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



IT 153037-25-3P 153037-26-4P 153037-28-6P  
 153037-32-2P 153037-49-1P 154116-31-1P  
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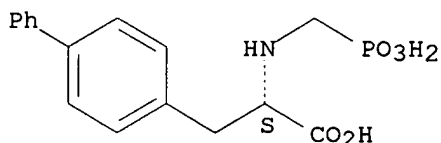
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(product; prepn. of phosphono-substituted tetrazole derivs. and analogs as ECE inhibitors)

RN 153037-25-3 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

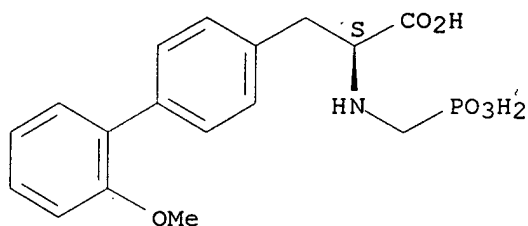
Absolute stereochemistry.



RN 153037-26-4 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 2'-methoxy-.alpha.-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

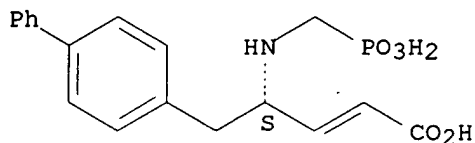


RN 153037-28-6 CAPLUS

CN 2-Pentenoic acid, 5-[1,1'-biphenyl]-4-yl-4-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

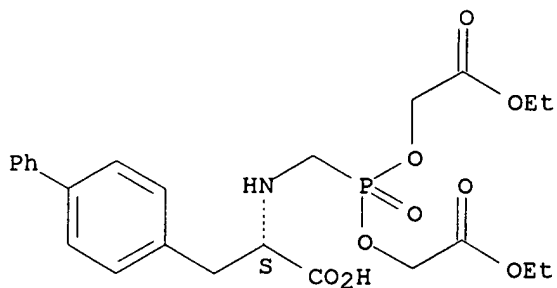
Double bond geometry unknown.



RN 153037-32-2 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[[bis(2-ethoxy-2-oxoethoxy)phosphinyl)methyl]amino]-, (S)- (9CI) (CA INDEX NAME)

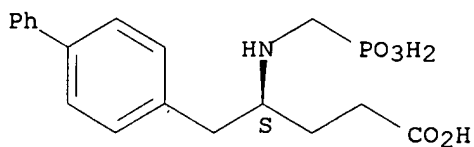
Absolute stereochemistry.



RN 153037-49-1 CAPLUS

CN [1,1'-Biphenyl]-4-pentanoic acid, .gamma.-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

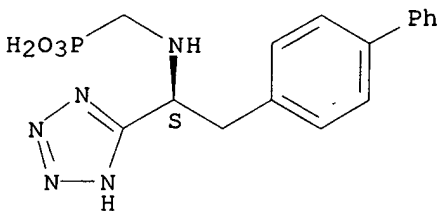
Absolute stereochemistry.



RN 154116-31-1 CAPLUS

CN Phosphonic acid, [[[1S]-2-[1,1'-biphenyl]-4-yl-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)

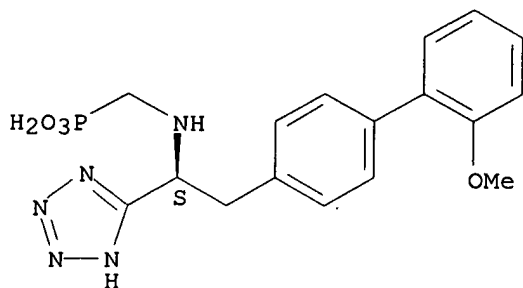
Absolute stereochemistry.



RN 154116-33-3 CAPLUS

CN Phosphonic acid, [[[2-(2'-methoxy[1,1'-biphenyl]-4-yl)-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

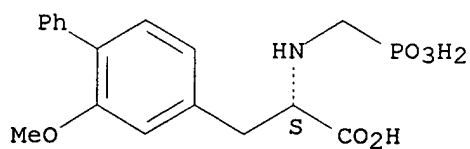
Absolute stereochemistry.



RN 161805-43-2 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 2-methoxy-.alpha.-  
[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

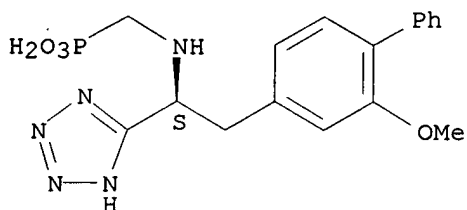
Absolute stereochemistry.



RN 161805-48-7 CAPLUS

CN Phosphonic acid, [[[2-(2-methoxy[1,1'-biphenyl]-4-yl)-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

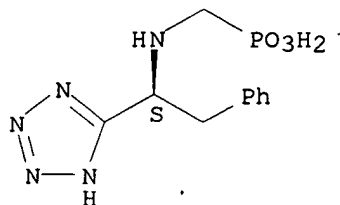
Absolute stereochemistry.



RN 161805-52-3 CAPLUS

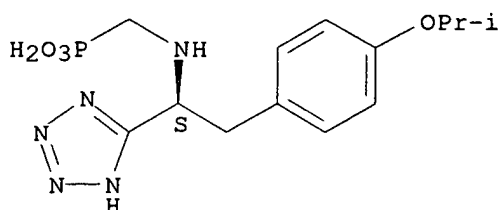
CN Phosphonic acid, [[[2-phenyl-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



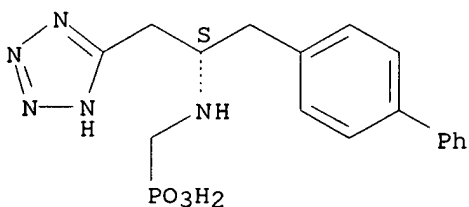
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Absolute stereochemistry.



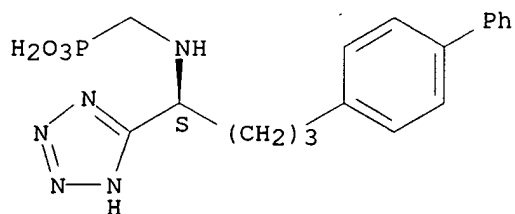
RN 182192-83-2 CAPLUS  
 CN Phosphonic acid, [[[1-([1,1'-biphenyl]-4-ylmethyl)-2-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182192-85-4 CAPLUS  
 CN Phosphonic acid, [[[4-[1,1'-biphenyl]-4-yl-1-(1H-tetrazol-5-yl)butyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





ACCESSION NUMBER: 1996:546615 CAPLUS  
 DOCUMENT NUMBER: 125:275882  
 TITLE: Phosphono-substituted tetrazole derivatives and  
 analogs as ECE inhibitors  
 INVENTOR(S): DeLombaert ,Stephane; Jeng, Arco Y.; Ksander, Gary M.  
 PATENT ASSIGNEE(S): Ciba-Geigy Corporation, USA  
 SOURCE: U.S., 25 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5550119	A	19960827	US 1995-403353	19950302
WO 9626729	A1	19960906	WO 1996-EP699	19960220
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9648786	A1	19960918	AU 1996-48786	19960220
PRIORITY APPLN. INFO.:			US 1995-403353	19950302
			WO 1996-EP699	19960220
OTHER SOURCE(S):			MARPAT 125:275882	
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

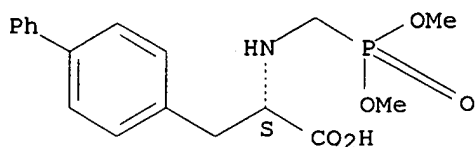
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IT **147862-23-5P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (intermediate; prepn. of phosphono-substituted tetrazole derivs. and  
 analogs as ECE inhibitors)

RN 147862-23-5 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid,  
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 ino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 153037-39-9P 182192-87-6P

RL: BAC (Biological activity or effector, except adverse); RCT  
 (Reactant);

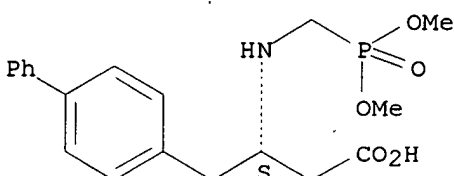
SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)

(product and intermediate; prepn. of phosphono-substituted tetrazole  
 derivs. and analogs as ECE inhibitors)

RN 153037-39-9 CAPLUS

CN [1,1'-Biphenyl]-4-butanoic acid,  
 .beta.-[[ (dimethoxyphosphinyl)methyl]amin  
 o]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

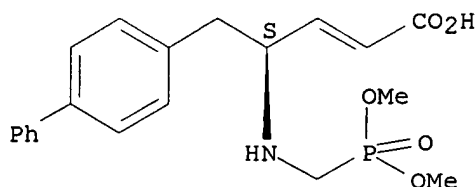


RN 182192-87-6 CAPLUS

CN 2-Pentenoic acid,  
 5-[1,1'-biphenyl]-4-yl-4-[[ (dimethoxyphosphinyl)methyl]a  
 mino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



IT 153037-25-3P 153037-26-4P 153037-28-6P  
 153037-32-2P 153037-49-1P 154116-31-1P  
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182192-85-4P

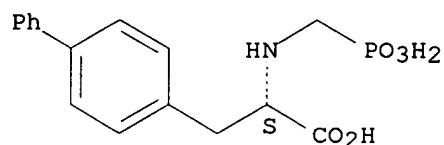
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(product; prepn. of phosphono-substituted tetrazole derivs. and analogs as ECE inhibitors)

RN 153037-25-3 CAPLUS

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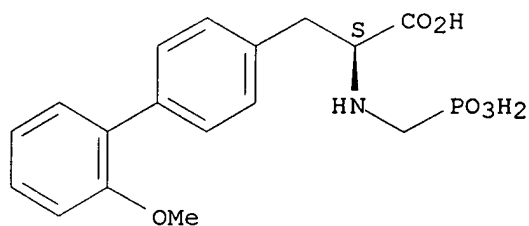
Absolute stereochemistry.



RN 153037-26-4 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 2'-methoxy-.alpha.-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

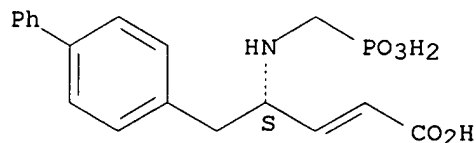


RN 153037-28-6 CAPLUS

CN 2-Pentenoic acid, 5-[1,1'-biphenyl]-4-yl-4-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

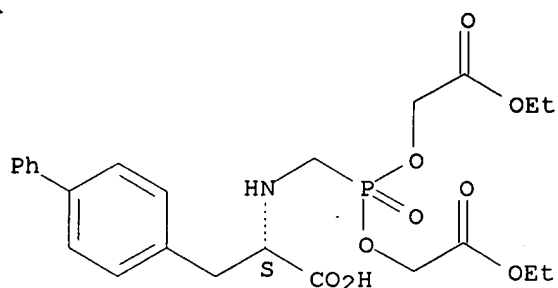
Double bond geometry unknown.



RN 153037-32-2 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[[bis(2-ethoxy-2-oxoethoxy)phosphinyl)methyl]amino]-, (S)- (9CI) (CA INDEX NAME)

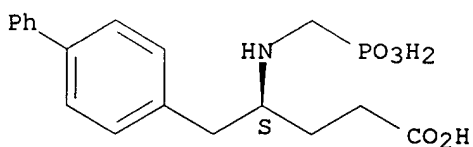
Absolute stereochemistry.



RN 153037-49-1 CAPLUS

CN [1,1'-Biphenyl]-4-pentanoic acid, .gamma.-[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

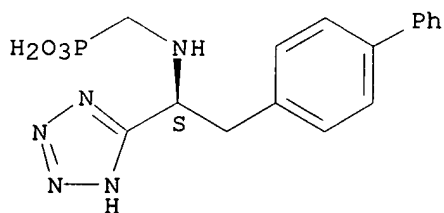
Absolute stereochemistry.



RN 154116-31-1 CAPLUS

CN Phosphonic acid, [[[1S)-2-[1,1'-biphenyl]-4-yl-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)

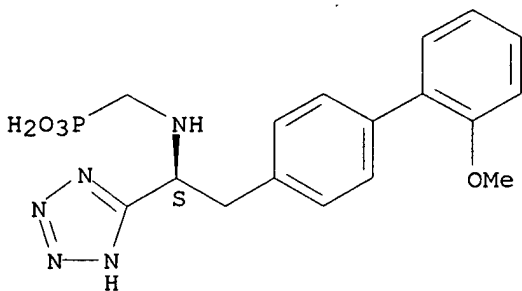
Absolute stereochemistry.



RN 154116-33-3 CAPLUS

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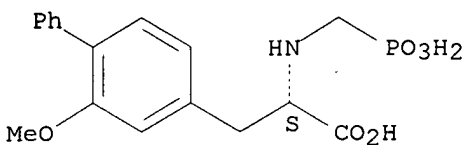
Absolute stereochemistry.



RN 161805-43-2 CAPLUS

CN [1,1'-Biphenyl]-4-propanoic acid, 2-methoxy-.alpha.-  
[(phosphonomethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

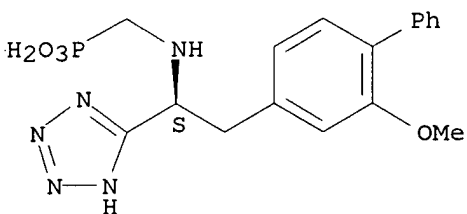
Absolute stereochemistry.



RN 161805-48-7 CAPLUS

CN Phosphonic acid, [[[2-(2-methoxy[1,1'-biphenyl]-4-yl)-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

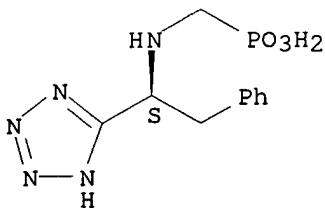
Absolute stereochemistry.



RN 161805-52-3 CAPLUS

CN Phosphonic acid, [[[2-phenyl-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

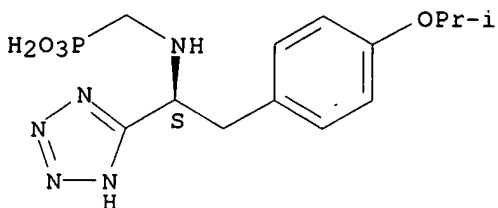
Absolute stereochemistry.



RN 161805-53-4 CAPLUS

CN Phosphonic acid, [[[2-[4-(1-methylethoxy)phenyl]-1-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

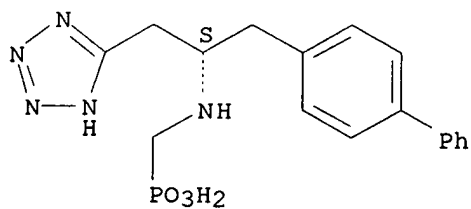
Absolute stereochemistry.



RN 182192-83-2 CAPLUS

CN Phosphonic acid, [[[1-([1,1'-biphenyl]-4-ylmethyl)-2-(1H-tetrazol-5-yl)ethyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

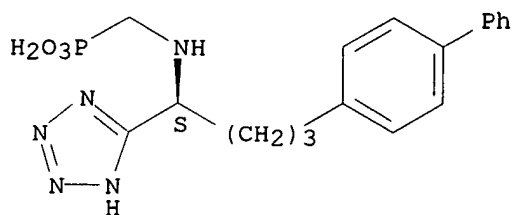
Absolute stereochemistry.



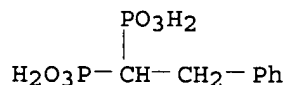
RN 182192-85-4 CAPLUS

CN Phosphonic acid, [[[4-[1,1'-biphenyl]-4-yl]-1-(1H-tetrazol-5-yl)butyl]amino]methyl]-, (S)- (9CI) (CA INDEX NAME)

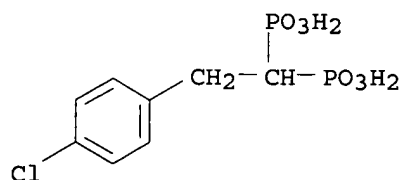
Absolute stereochemistry.



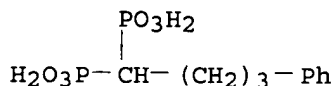
SESSION NUMBER: 1987:459121 CAPLUS  
 DOCUMENT NUMBER: 107:59121  
 TITLE: gem-Diphosphonate and gem-phosphonate-phosphate compounds with specific high density lipoprotein inducing activity  
 AUTHOR(S): Nguyen Lan Mong; Niesor, Eric; Bentzen, Craig L.  
 CORPORATE SOURCE: Symphar S. A., Geneva, Switz.  
 SOURCE: J. Med. Chem. (1987), 30(8), 1426-33  
 CODEN: JMCMAR; ISSN: 0022-2623  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 107:59121  
 AB Title compds. [(RO)2P(O)]2CR1R2 [R = Me, Et, Pr, Me2CH, Bu; R1 = H, OH; R2 = alkyl, (un)substituted aryl] and (RO)2P(O)CR1R2OP(O)(OR)2 (I; same R-R2) were prepd. and examd. for activity in specifically inducing plasma high-d. lipoproteins (HDL) and HDL-cholesterol (HDL-C) in normal rats. Screening numerous compds. allowed detn. of structural variations leading to optimal plasma lipid-altering activity and antiatherosclerotic potential. I (R = Me; R1 = H; R2 = 4-ClC6H4) (SR-202, mifobate) was selected for further pharmacol. and subsequent clin. development.  
 IT 10596-19-7P 76541-77-0P 76541-78-1P  
 89187-56-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and antiatherosclerotic activity of)  
 RN 10596-19-7 CAPLUS  
 CN Phosphonic acid, (2-phenylethylidene)bis- (9CI) (CA INDEX NAME)



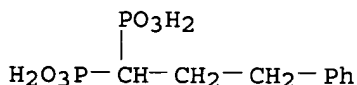
RN 76541-77-0 CAPLUS  
 CN Phosphonic acid, [2-(4-chlorophenyl)ethylidene]bis- (9CI) (CA INDEX NAME)



RN 76541-78-1 CAPLUS  
 CN Phosphonic acid, (4-phenylbutylidene)bis- (9CI) (CA INDEX NAME)



RN 89187-56-4 CAPLUS  
 CN Phosphonic acid, (3-phenylpropylidene)bis- (9CI) (CA INDEX NAME)



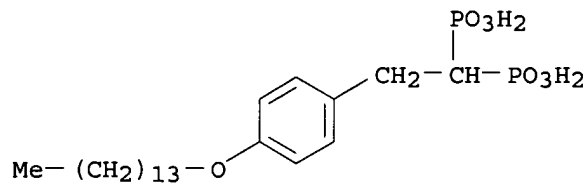
ACCES

108816-95-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and esterification of)

RN 108816-95-1 CAPLUS

CN Phosphonic acid, [2-[4-(tetradecyloxy)phenyl]ethylidene]bis- (9CI) (CA  
INDEX NAME)





IT **Atherosclerosis**  
 (gem-diphosphonates and gem-phosphonate phosphates, high-d. lipoprotein  
 in relation to treatment of)

IT Condensation reaction  
 (of alkyl phosphites with acid chlorides and phosphonates)

IT 100-39-0, Benzyl bromide 103-63-9, 2-Phenethyl bromide 588-63-6  
 589-10-6 637-59-2, 3-Phenylpropyl bromide 108003-51-6  
 RL: RCT (Reactant)  
 (alkylation by, of gem-tetraalkyl diphosphonate)

IT 104-83-6, p-Chlorobenzyl chloride  
 RL: RCT (Reactant)  
 (alkylation by, of gem-tetraalkyl diphosphonates)

IT 1660-94-2  
 RL: RCT (Reactant)  
 (alkylation of, by benzyl bromide)

IT 1660-95-3 6997-56-4  
 RL: RCT (Reactant)  
 (alkylation of, by chlorobenzyl chloride)

IT 50870-71-8  
 RL: RCT (Reactant)  
 (alkylation of, with phenylpropyl bromide)

IT 7664-38-2, Phosphoric acid, uses and miscellaneous  
 RL: USES (Uses)  
 (antiatherosclerotic agents, high-d. lipoproteins in relation to)

IT 62443-00-9  
 RL: RCT (Reactant)  
 (bromination of)

IT 121-45-9, Trimethyl phosphite  
 RL: RCT (Reactant)  
 (condensation reaction of, with acid chlorides)

IT 102-85-2, Tributyl phosphite 116-17-6, Triisopropyl phosphite  
 923-99-9, Tripropyl phosphite  
 RL: RCT (Reactant)  
 (condensation reaction of, with phosphonate)

IT 79-30-1 122-52-1, Triethyl phosphite 3283-12-3 7065-46-5  
 RL: RCT (Reactant)  
 (condensation reaction of, with phosphonates)

IT 108816-97-3  
 RL: RCT (Reactant)  
 (condensation reaction of, with tri-Bu phosphite)

IT 10570-46-4  
 RL: RCT (Reactant)  
 (condensation reaction of, with tri-Et phosphite)

IT 89-75-8 98-88-4 100-07-2 112-67-4, Palmitoyl chloride 122-01-0,  
 4-Chlorobenzoyl chloride 142-61-0 329-15-7 403-43-0, 4-Fluorobenzoyl  
 chloride 609-65-4 618-46-2 874-60-2, 4-Methylbenzoyl chloride  
 1711-09-7 2243-83-6 2719-27-9 4521-61-3 5542-60-9 14002-51-8  
 22328-43-4 36293-05-7 40919-11-7 63293-86-7 81928-54-3  
 RL: RCT (Reactant)  
 (condensation reaction of, with tri-Me phosphite)

IT 108816-96-2  
 RL: RCT (Reactant)  
 (condensation reaction of, with tri-Pr phosphite)

IT 41097-24-9  
 RL: RCT (Reactant)  
 (condensation reaction of, with triisopropyl phosphite)

IT 10419-59-7P **10596-19-7P** 32249-59-5P 32249-63-1P  
 53235-98-6P 76541-68-9P 76541-69-0P 76541-70-3P 76541-75-8P  
 76541-76-9P **76541-77-0P** **76541-78-1P** 76541-79-2P  
 76541-80-5P 76541-81-6P 76552-10-8P 81928-58-7P 89187-47-3P  
 89187-49-5P **89187-56-4P** 89187-57-5P 108816-47-3P  
 108816-48-4P 108816-49-5P 108816-50-8P 108816-51-9P 108816-52-0P  
 108816-53-1P 108816-54-2P 108816-55-3P 108816-56-4P 108816-57-5P  
 108816-58-6P 108816-59-7P 108816-60-0P 108816-61-1P 108816-62-2P

108816-63-3P	108816-64-4P	108816-65-5P	108816-66-6P	108816-67-7P
108816-68-8P	108816-69-9P	108816-70-2P	108816-71-3P	108816-72-4P
108816-73-5P	108816-74-6P	108816-75-7P	108816-76-8P	108816-77-9P
108816-78-0P	108816-79-1P	108816-80-4P	108816-81-5P	108816-82-6P
108816-83-7P	108816-84-8P	108816-85-9P	108816-86-0P	108816-87-1P
108816-88-2P	108816-89-3P	108834-48-6P	108834-49-7P	108834-50-0P
108834-51-1P	108868-05-9P			

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and antiatherosclerotic activity of)

IT 1490-12-6P 6918-58-7P 10570-48-6P 18106-71-3P 26583-87-9P  
 33493-30-0P 33493-32-2P 51463-64-0P 58879-27-9P 68963-39-3P  
 76387-49-0P 81928-53-2P 81928-55-4P 81928-56-5P 89187-59-7P  
 89187-60-0P 89187-63-3P 89198-46-9P 108130-19-4P 108816-90-6P  
 108816-91-7P 108816-92-8P 108816-93-9P 108834-52-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and condensation reaction of, with di-Me phosphite)

IT **108816-95-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and esterification of)

IT 59216-73-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and salt formation of)

=>

DOCUMENT NUMBER: 127:298722  
 TITLE: **Pharmaceutical** preparation for the treatment of blood coagulation disorders  
 INVENTOR(S): Turecek, Peter; Schwarz, Hans Peter; Eibl, Johann  
 PATENT ASSIGNEE(S): Immuno Aktiengesellschaft, Austria  
 SOURCE: Eur. Pat. Appl., 31 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 796623	A2	19970924	EP 1997-890051	19970318
EP 796623	A3	20000517		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, IE, IT, LI, NL, SE				
AT 9600518	A	19980615	AT 1996-518	19960320
AT 404673	B	19990125		
AT 9601573	A	20000515	AT 1996-1573	19960904
CA 2200394	AA	19970920	CA 1997-2200394	19970319
AU 9716451	A1	19970925	AU 1997-16451	19970320
US 5866122	A	19990202	US 1997-821763	19970320
JP 10045620	A2	19980217	JP 1997-108013	19970321
US 6039945	A	20000321	US 1998-165745	19981006
PRIORITY APPLN. INFO.:			AT 1996-518	19960320
			AT 1996-1573	19960904
			AT 1996-1673	19960920
			US 1997-821763	19970320

AB Patients with hemophilia A who develop inhibitory antibodies to coagulation factor VIII are effectively treated with a stable phospholipid-free compn. contg. a complex of .gtoreq.2 coagulation factors

which are components of a prothrombinase or preprothrombinase; .gtoreq.1 of these factors must be activated. The factors may be selected from coagulation factors II, V, Va, X, and Xa, and are purified until free from

endogenous phospholipids which might cause thromboembolic side effects. The compn. is not subject to premature thrombin formation; thrombin is formed only at the site of bleeding as a result of contact with cellular phospholipids. Thus, a lyophilized fraction contg. multiple coagulation factors was subjected to adsorption on Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>, (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pptn., and chromatog. on Sephadex G-25, and the coagulation factors were sepd. by ion-exchange chromatog. on DEAE-Sepharose FF; factor II was further purified by hydrophobic interaction chromatog. and ultrafiltration. A **pharmaceutical** formulation contained highly purified factor II, factor Xa, and antithrombin III in citrate buffer (pH 7.0) contg. NaCl (8 g/L), and could be lyophilized without significant loss of activity.

IT 194554-71-7, **Tissue factor** pathway inhibitor

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (antidotes for; **pharmaceutical** prepn. for treatment of blood coagulation disorders)

RN 194554-71-7 CAPLUS

CN Proteinase inhibitor, TFPI (9CI) (CA INDEX NAME)

DOCUMENT NUMBER: 127:298722  
 TITLE: **Pharmaceutical** preparation for the treatment of blood coagulation disorders  
 INVENTOR(S): Turecek, Peter; Schwarz, Hans Peter; Eibl, Johann  
 PATENT ASSIGNEE(S): Immuno Aktiengesellschaft, Austria  
 SOURCE: Eur. Pat. Appl., 31 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 796623	A2	19970924	EP 1997-890051	19970318
EP 796623	A3	20000517		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, IE, IT, LI, NL, SE				
AT 9600518	A	19980615	AT 1996-518	19960320
AT 404673	B	19990125		
AT 9601573	A	20000515	AT 1996-1573	19960904
CA 2200394	AA	19970920	CA 1997-2200394	19970319
AU 9716451	A1	19970925	AU 1997-16451	19970320
US 5866122	A	19990202	US 1997-821763	19970320
JP 10045620	A2	19980217	JP 1997-108013	19970321
US 6039945	A	20000321	US 1998-165745	19981006
PRIORITY APPLN. INFO.:			AT 1996-518	19960320
			AT 1996-1573	19960904
			AT 1996-1673	19960920
			US 1997-821763	19970320
AB	Patients with hemophilia A who develop inhibitory antibodies to coagulation factor VIII are effectively treated with a stable phospholipid-free compn. contg. a complex of .gtoreq.2 coagulation factors which are components of a prothrombinase or preprothrombinase; .gtoreq.1 of these factors must be activated. The factors may be selected from coagulation factors II, V, Va, X, and Xa, and are purified until free from endogenous phospholipids which might cause thromboembolic side effects. The compn. is not subject to premature thrombin formation; thrombin is formed only at the site of bleeding as a result of contact with cellular phospholipids. Thus, a lyophilized fraction contg. multiple coagulation factors was subjected to adsorption on Ca3(PO4)2, (NH4)2SO4 pptn., and chromatog. on Sephadex G-25, and the coagulation factors were sepd. by ion-exchange chromatog. on DEAE-Sepharose FF; factor II was further purified by hydrophobic interaction chromatog. and ultrafiltration. A <b>pharmaceutical</b> formulation contained highly purified factor II, factor Xa, and antithrombin III in citrate buffer (pH 7.0) contg. NaCl (8 g/L), and could be lyophilized without significant loss of activity.			
IT	194554-71-7, <b>Tissue factor</b> pathway inhibitor RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (antidotes for; <b>pharmaceutical</b> prepn. for treatment of blood coagulation disorders)			
RN	194554-71-7 CAPLUS			
CN	Proteinase inhibitor, TFPI (9CI) (CA INDEX NAME)			

ACCESSION NUMBER: 1999:21682 CAPLUS  
 DOCUMENT NUMBER: 130:90529  
 TITLE: Therapeutic derivatives of diphosphonates, and a method for preparing them  
 INVENTOR(S): Hartmann, John F.; Farcasiu, Dan  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 206,113, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5854227	A	19981229	US 1995-473787	19950607
WO 9640156	A1	19961219	WO 1996-US9271	19960606
W: AU, BR, CA, CZ, HU, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2224067	AA	19961219	CA 1996-2224067	19960606
AU 9660949	A1	19961230	AU 1996-60949	19960606
EP 831845	A1	19980401	EP 1996-918247	19960606
R: DE, ES, FR, GB, IT, SE				
PRIORITY APPLN. INFO.:			US 1994-206113	19940304
			US 1995-473787	19950607
			WO 1996-US9271	19960606

OTHER SOURCE(S): MARPAT 130:90529

AB Chemotherapeutic agents having utility in **treating** infectious diseases, e.g. periodontal disease, certain urinary tract infections, infectious urinary tract stones, and bone **cancer**, are obtained by combining chem. a diphosphonate compd. with a therapeutic agent effective against the foregoing diseases.

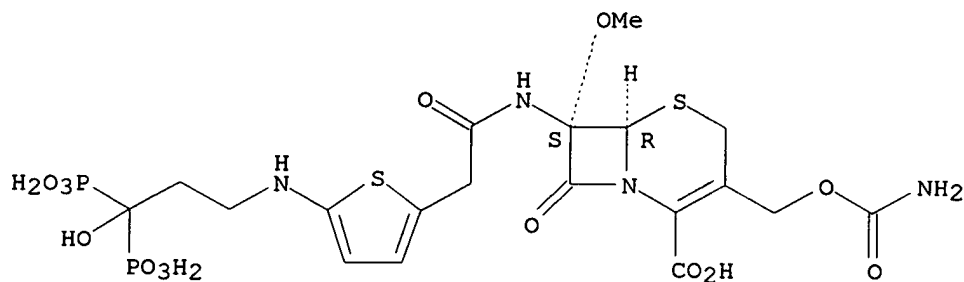
IT 186520-45-6P 186520-47-8P 186520-67-2P  
 186520-71-8P 186520-76-3P 219129-76-7P  
 219129-81-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; therapeutic derivs. of diphosphonates, and a method for prepg. them)

RN 186520-45-6 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[aminocarbonyl]oxy]methyl]-7-[[[5-[(3-hydroxy-3,3-diphosphonopropyl)amino]-2-thienyl]acetyl]amino]-7-methoxy-8-oxo-, (6R,7S)- (9CI) (CA INDEX NAME)

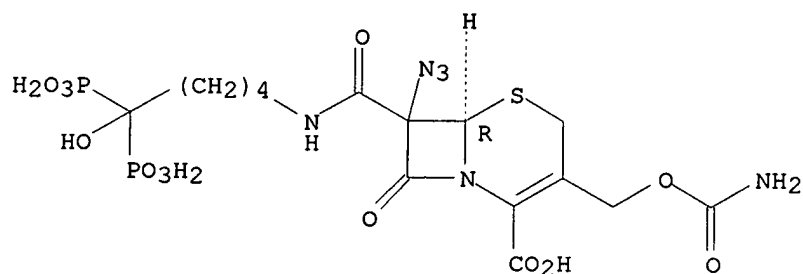
Absolute stereochemistry.



RN 186520-47-8 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
3-[[ (aminocarbonyl)oxy)methyl]-7-azido-7-[[ (5-hydroxy-5,5-  
diphosphonopentyl)amino]carbonyl]-8-oxo-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

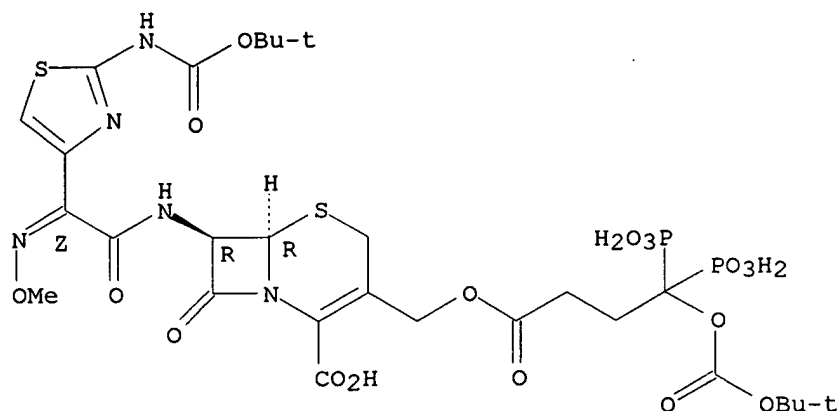


RN 186520-67-2 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
7-[[ (2Z)-[2-[[ (1,1-dimethylethoxy)carbonyl]amino]-4-  
thiazolyl] (methoxyimino)acetyl]amino]-3-[[4-[[ (1,1-  
dimethylethoxy)carbonyl]oxy]-1-oxo-4,4-diphosphonobutoxy]methyl]-8-oxo-,  
(6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



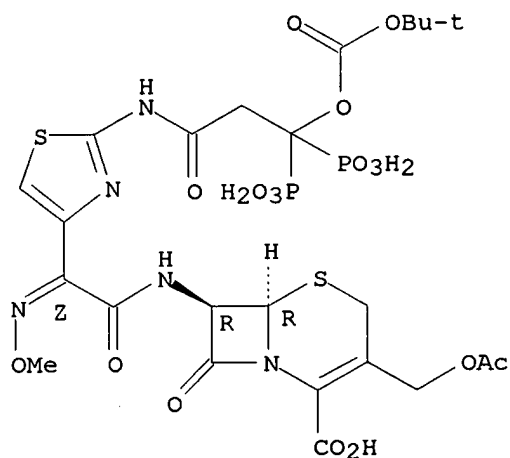
RN 186520-71-8 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

3-[(acetyloxy)methyl]-7-[[ (2Z)-[2-[[3-[[ (1,1-dimethylethoxy) carbonyl]oxy]-  
1-oxo-3,3-diphosphonopropyl]amino]-4-thiazolyl] (methoxyimino)acetyl]amino]-  
8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

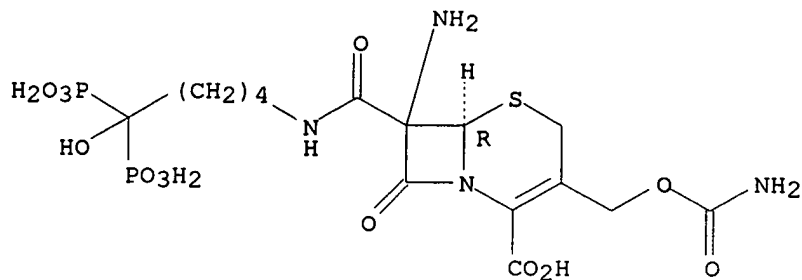


RN 186520-76-3 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

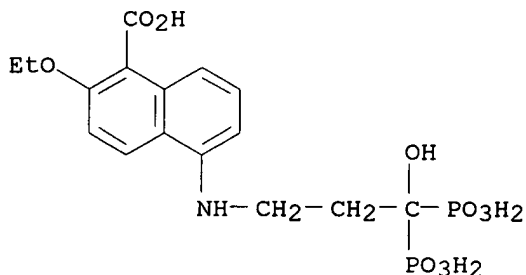
7-amino-3-[[ (aminocarbonyl)oxy]methyl]-7-[[ (5-hydroxy-5,5-  
diphosphonopentyl)amino]carbonyl]-8-oxo-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 219129-76-7 CAPLUS

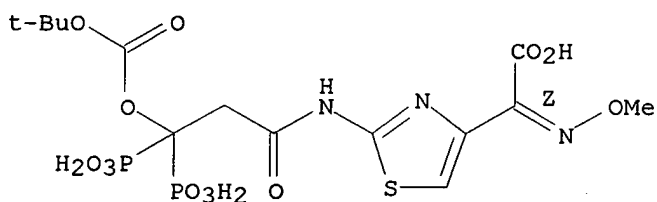
CN 1-Naphthalenecarboxylic acid, 2-ethoxy-5-[(3-hydroxy-3,3-diphosphonopropyl)amino]- (9CI) (CA INDEX NAME)



RN 219129-81-4 CAPLUS

CN 4-Thiazoleacetic acid,  
2-[[[3-[(1,1-dimethylethoxy)carbonyl]oxy]-1-oxo-3,3-diphosphonopropyl]amino]-.alpha.-(methoxyimino)-, (.alpha.Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



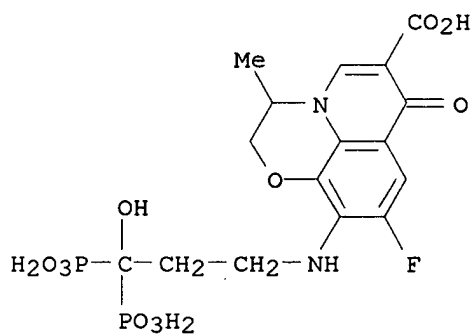
IT 186520-17-2 186520-17-2D, esters 186520-21-8  
186520-21-8D, esters 186520-36-5 186520-36-5D,  
esters 186520-37-6 186520-37-6D, esters  
186520-39-8 186520-39-8D, esters 186520-45-6D,  
esters 186520-47-8D, esters 186520-48-9  
186520-48-9D, esters 186520-49-0 186520-49-0D,  
esters

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(therapeutic derivs. of diphosphonates, and a method for prepg. them)



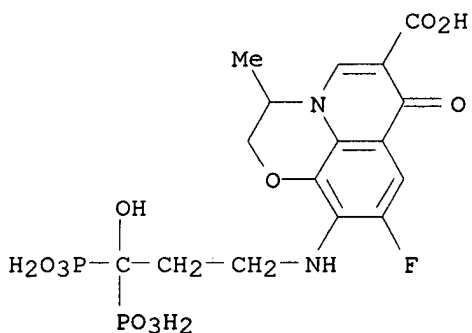
RN 186520-17-2 CAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,

9-fluoro-2,3-dihydro-10-[(3-hydroxy-3,3-diphosphonopropyl) amino]-3-methyl-  
7-oxo- (9CI) (CA INDEX NAME)

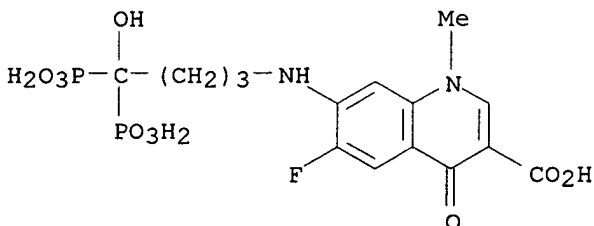
RN 186520-17-2 CAPLUS

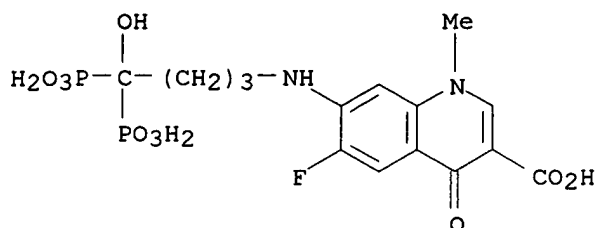
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,

9-fluoro-2,3-dihydro-10-[(3-hydroxy-3,3-diphosphonopropyl) amino]-3-methyl-  
7-oxo- (9CI) (CA INDEX NAME)

RN 186520-21-8 CAPLUS

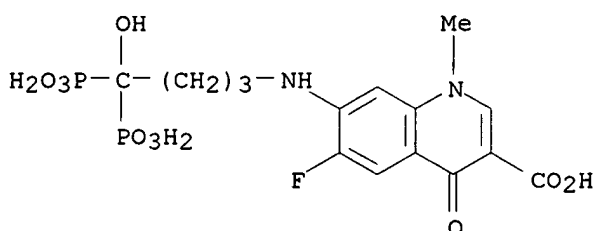
CN 3-Quinolinecarboxylic acid, 6-fluoro-1,4-dihydro-7-[(4-hydroxy-4,4-diphosphonobutyl) amino]-1-methyl-4-oxo- (9CI) (CA INDEX NAME)





RN 186520-21-8 CAPLUS

CN 3-Quinolinecarboxylic acid, 6-fluoro-1,4-dihydro-7-[(4-hydroxy-4,4-diphosphonobutyl)amino]-1-methyl-4-oxo- (9CI) (CA INDEX NAME)

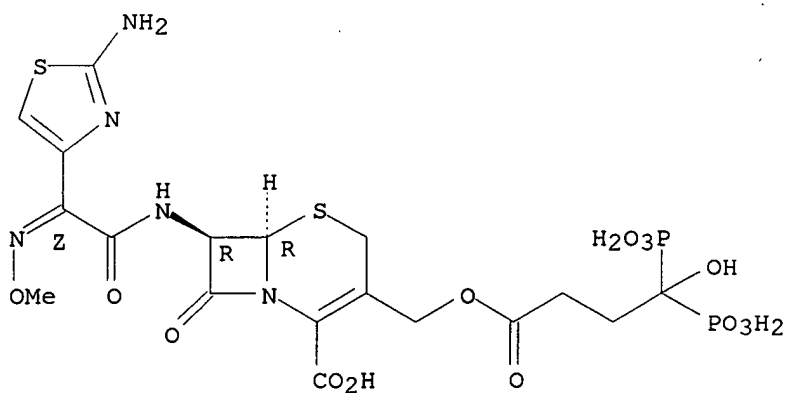


RN 186520-36-5 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

7-[[ (2Z)-(2-amino-4-thiazolyl) (methoxyimino) acetyl] amino]-3-[(4-hydroxy-1-oxo-4,4-diphosphonobutoxy)methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

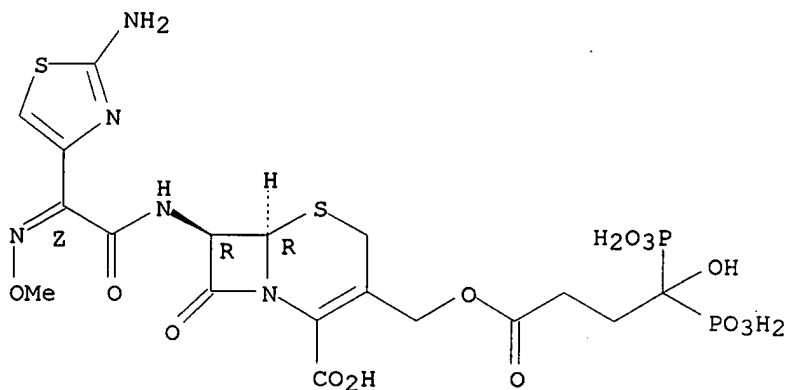


RN 186520-36-5 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

7-[[ (2Z)-(2-amino-4-thiazolyl) (methoxyimino) acetyl] amino]-3-[(4-hydroxy-1-oxo-4,4-diphosphonobutoxy)methyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

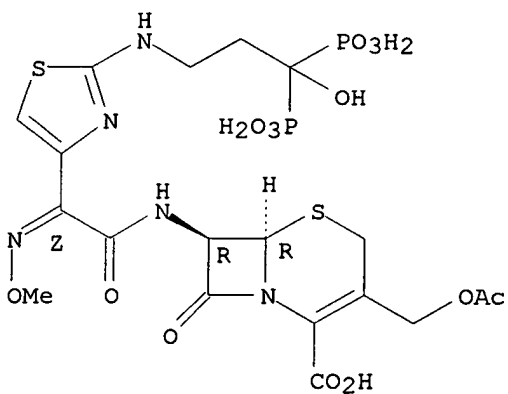


RN 186520-37-6 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

3-[(acetyloxy)methyl]-7-[[ (2Z)-[2-[(3-hydroxy-3,3-diphosphonopropyl)amino]-4-thiazolyl] (methoxyimino)acetyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

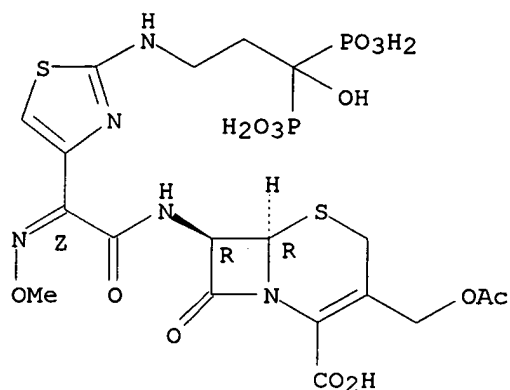


RN 186520-37-6 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

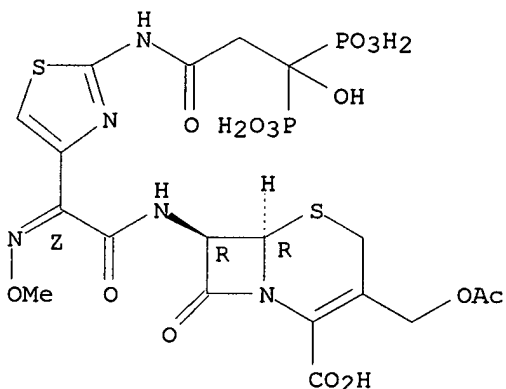
3-[(acetyloxy)methyl]-7-[[ (2Z)-[2-[(3-hydroxy-3,3-diphosphonopropyl)amino]-4-thiazolyl] (methoxyimino)acetyl]amino]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



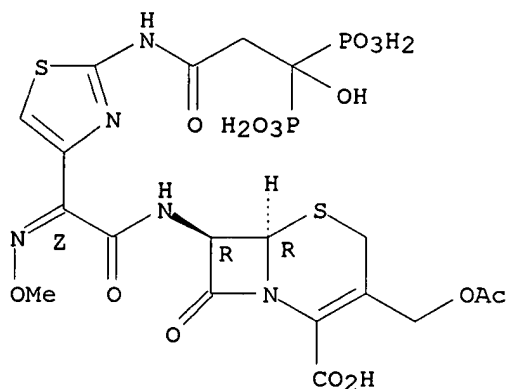
RN 186520-39-8 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[(acetyloxy)methyl]-7-[[ (2Z)-[2-[(3-hydroxy-1-oxo-3,3-  
 diphosphonopropyl)amino]-4-thiazolyl] (methoxyimino)acetyl]amino]-8-oxo-,  
 (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



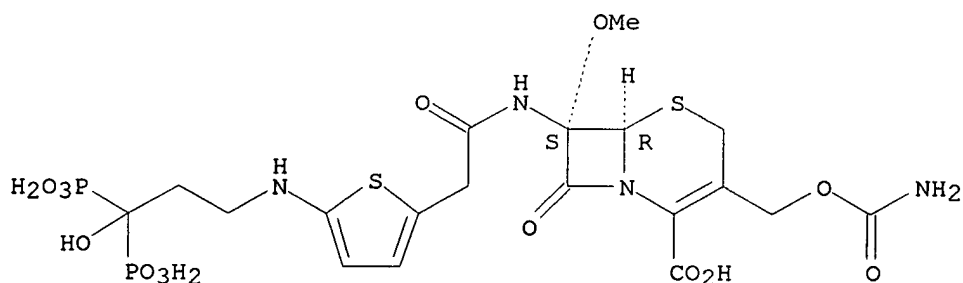
RN 186520-39-8 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[(acetyloxy)methyl]-7-[[ (2Z)-[2-[(3-hydroxy-1-oxo-3,3-  
 diphosphonopropyl)amino]-4-thiazolyl] (methoxyimino)acetyl]amino]-8-oxo-,  
 (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



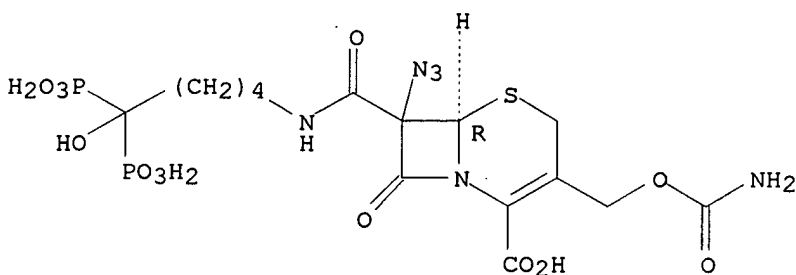
RN 186520-45-6 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[[ (aminocarbonyl)oxy]methyl]-7-[[[5-[(3-hydroxy-3,3-  
 diphosphonopropyl)amino]-2-thienyl]acetyl]amino]-7-methoxy-8-oxo-,  
 (6R,7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



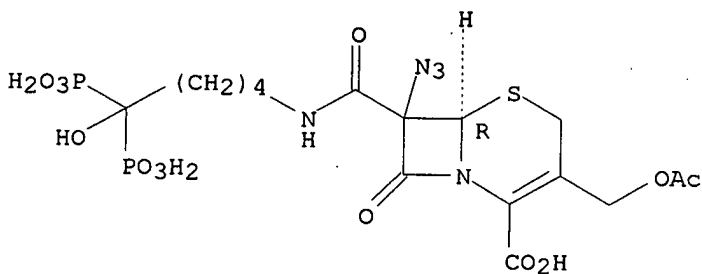
RN 186520-47-8 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[[ (aminocarbonyl)oxy]methyl]-7-azido-7-[[[5-hydroxy-5,5-  
 diphosphonopentyl]amino]carbonyl]-8-oxo-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



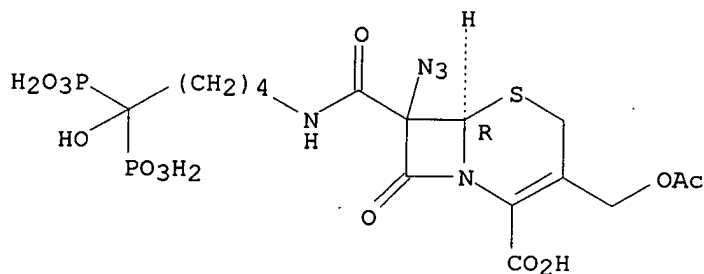
RN 186520-48-9 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[(acetyloxy)methyl]-7-azido-7-[[ (5-hydroxy-5,5-  
 diphosphonopentyl)amino]carbonyl]-8-oxo-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



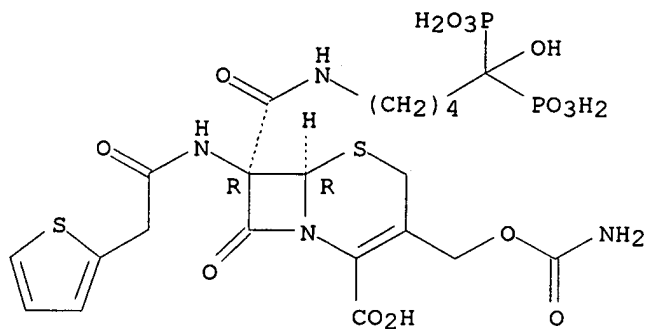
RN 186520-48-9 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[(acetyloxy)methyl]-7-azido-7-[[ (5-hydroxy-5,5-  
 diphosphonopentyl)amino]carbonyl]-8-oxo-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186520-49-0 CAPLUS  
 CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[[ (aminocarbonyl)oxy]methyl]-7-[[ (5-hydroxy-5,5-  
 diphosphonopentyl)amino]carbonyl]-8-oxo-7-[(2-thienylacetyl)amino]-,  
 (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186520-49-0 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,  
 3-[[ (aminocarbonyl)oxy]methyl]-7-[[ (5-hydroxy-5,5-  
 diphosphonopentyl)amino]carbonyl]-8-oxo-7-[(2-thienylacetyl)amino]-,  
 (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

